HIV Molecular Immunology 2002

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Preface

Scope and Purpose of the HIV Molecular Immunology Database

HIV Molecular Immunology is a companion volume to *Human Retroviruses and AIDS Genetic Sequence Compendium*. This publication, the 2002 issue, is the printed version of the Web-based HIV Immunology Database (`http://hiv-web.lanl.gov/immunology`). The web interface for this relational database has many search options, as well as interactive tools to help immunologists design reagents and interpret their results.

The data included in this database is extracted from the HIV immunology literature. HIV-specific B-cell and T-cell responses are summarized and annotated. Immunological responses are divided into three sections, CTL, T helper, and antibody. Within these sections, defined epitopes are organized by protein and binding sites within each protein, moving from left to right through the coding regions spanning the HIV genome. We include human responses to natural HIV infections, as well as vaccine studies in a range of animal models and human trials. Responses that are not specifically defined, such as responses to whole proteins or monoclonal antibody responses to discontinuous epitopes, are summarized at the end of each protein sub-section. Studies describing general HIV responses to the virus, but not to any specific protein, are included at the end of each section.

The annotation includes information such as cross-reactivity, escape mutations, antibody sequence, TCR usage, functional domains that overlap with an epitope, immune response associations with rates of progression and therapy, and how specific epitopes were experimentally defined. Basic information such as HLA specificities for T-cell epitopes, isotypes of monoclonal antibodies, and epitope sequences are included whenever possible. All studies that we can find that incorporate the use of a specific monoclonal antibody are included in the entry for that antibody. A single T cell epitope can have multiple entries, generally one entry per study.

Finally, maps of all defined linear epitopes relative to the HXB2 reference proteins are provided. Alignments of CTL, helper T-cell, and antibody epitopes are available through the search interface on our web site at `http://hiv-web.lanl.gov/immunology`.

Only responses to HIV-1 and HIV-2 are included in the database. CTL responses to SIVs have been periodically summarized in our review section by Dr. Dave Watkins and colleagues. (For their most recent review, please see: Where Have All The Monkeys Gone?: Evaluating SIV-Specific CTL in the Post-Mamu-A*01 Era David H. O'Connor, Todd M. Allen, and David I. Watkins, in the 2001 HIV Immunology compendium). Dr. Christian Brander and colleagues annually provide a concise listing of optimal CTL epitopes. Additional reviews that our editorial board deems of general interest to the HIV research immunology community are solicited each year. This year's reviews are printed in the first section of this database; reviews from previous years can be found at: `http://www.hiv.lanl.gov/content/hiv-db/REVIEWS/reviews.html`.

Comments on the database or requests for the hard copy can be sent via email to `immuno@t10.lanl.gov`.

Citing the Database

This publication may be cited as

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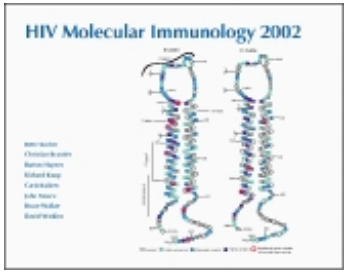
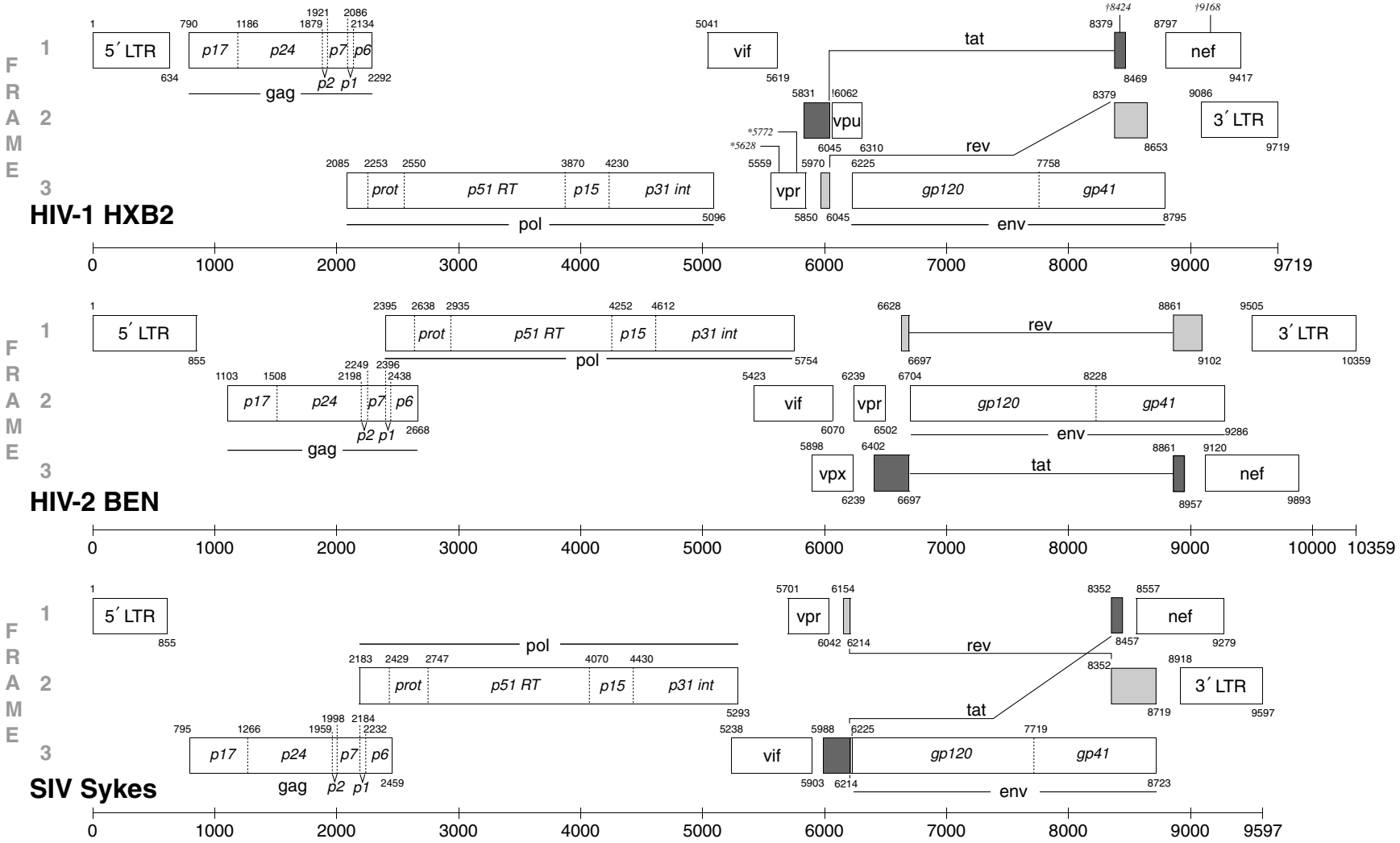
About the Cover



The illustration used for the cover of this year's immunology compendium highlights the location of the most variable amino acids in gp41, and was extracted from the review: Mutational Analyses and Natural Variability of the gp41 Ectodomain, by Rogier W. Sanders, Bette Korber, Min Lu, Ben Berkhout, and John P. Moore (this volume).

About the PDF

The complete *HIV Molecular Immunology 2002* is available in Adobe Portable Document Format (PDF) from our website, `http://hiv-web.lanl.gov/immunology`. The PDF version is hypertext enabled and features 'clickable' table-of-contents, indexes, references and links to external web sites.



Landmarks of the HIV-1, HIV-2, and SIV genomes. The gene start, indicated by the small number in the upper left corner of each rectangle normally records the position of the `a` in the `atg` start codon for that gene while the number in the lower right records the last position of the stop codon. For *pol*, the start is taken to be the first `t` in the sequence `ttttttag` which forms part of the stem loop that potentiates ribosomal slippage on the RNA and a resulting −1 frameshift and the translation of the Gag-Pol polyprotein. The *tat* and *rev* spliced exons are shown as shaded rectangles. In HXB2, *5628 and *5772 mark positions of frameshifts in the *vpr* gene; !6062 indicates a defective `acg` start codon in *vpu*; †8424 and †9168 mark premature stop codons in *tat* and *nef*. See Korber *et al.*, Numbering Positions in HIV Relative to HXB2CG, in *Human Retroviruses and AIDS*, 1998, p. 102. Available from `http://hiv-web.lanl.gov/HTML/reviews/HXB2.html`.

HIV/SIV Proteins

Name	Size	Function	Localization
Gag MA	p17	membrane anchoring; env interaction; nuclear transport of viral core. (myristylated protein)	virion
CA	p24	core capsid	virion
NC	p7	nucleocapsid, binds RNA	virion
	p6	binds Vpr	virion
Protease (PR)	p15	gag/pol cleavage and maturation	virion
Reverse Transcriptase (RT)	p66, p51	reverse transcription	virion
RNase H	(heterodimer)	RNAse H activity	virion
Integrase (IN)		DNA provirus integration	virion
Env	gp120/gp41	external viral glycoproteins bind to CD4 and chemokine co-receptors	plasma membrane, virion envelope
Tat	p16/p14	viral transcriptional transactivator	primarily in nucleolus/nucleus
Rev	p19	RNA transport, stability and utilization factor (phosphoprotein)	primarily in nuleolus/nucleus shuttling between nucleolus and cytoplasm
Vif	p23	viral infectivity factor, inhibits minus-strand viral DNA hypermutation	cytoplasm (cytosol, membranes), virion
Vpr	p10-15	promotes nuclear localization of preintegration complex, inhibits cell division, arrests infected cells at G2/M	virion nucleus (nuclear membrane?)
Vpu	p16	promotes extracellular release of viral particles; degrades CD4 in the ER; (phosphoprotein only in HIV-1 and SIVcpz)	integral membrane protein
Nef	p27-p25	CD4 and class I downregulation (myristylated protein)	plasma membrane, cytoplasm, (virion?)
Vpx	p12-16	Vpr homolog present in HIV-2 and some SIVs absent in HIV-1	virion (nucleus?)
Tev	p28	tripartite tat-env-rev protein (also named Tnv)	primarily in nucleolus/nucleus

Abbreviations

Common abbreviations used in this database.

Abbrev.	Meaning
Ab	Antibody
ADCC	Antibody-Dependent Cell-medicated Cytotoxicity
ADE	Antibody-Dependent Enhancement
APC	Antigen Presenting Cell
AZT	Azidothymidine
CD4BS	CD4 Binding Site
CD4i	Antibody that has enhanced binding to gp120 in the presence of SCD4 (CD4 induced)
CSF	Cerebrospinal Fluid
CTL	Cytotoxic T Lymphocyte
CTLp	CTL precursor
DTT	Dithiothrietol
EIA	Enzyme Immuno Assay
ELISA	Enzyme Linked ImmunoSorbent Assay
ER	Endoplasmic reticulum
Fabs	Fragment Antigen Binding-univalent antibody fragment
FIV	Feline Immunodeficiency Virus
gp	Glycoprotein
HIV	Human Immunodeficiency Virus
HLA	Human Leukocyte Antigens
HLA-MHC	Human Leukocyte Antigens-Major Histocompatibility Complex
IFN	Interferon
IL	Interleukin
IN	Integrase
Ig	Immunoglobulin
MAb	Monoclonal Antibody
MHC	Major Histocompatibility Complex
MRC	Medical Research Council, UK
NAb	Neutralizing Antibody
NIBSC	National Institute for Biological Standards and Control, UK
NIH	National Institutes of Health
PBLs	Peripheral Blood Lymphocyte
PBMC	Peripheral Blood Mononuclear Cell
PR	Protease
RAC	Ricin A Chain
rec/r	recombinant
RIP	Recombinant Identification Program
RIPA	Radio Immuno Precipitation assay
rsgp160	recombinant soluble gp160
RT	Reverse Transcriptase
sCD4	soluble CD4
SDS	Sodium Duodecyl Sulfate
SIV	Simian Immunodeficiency Virus
Th	T-helper cell
TNF	Tumor Necrosis Factor
VLP	Virus like particle, assembled from p55 gag
VV	Vaccinia virus
WB	Western Blot

Part I

Review Articles

Total Assessment of HIV-Specific CTL Responses: Epitope Clustering, Processing Preferences, and the Impact of HIV Sequence Heterogeneity

Nicole Frahm[1], Philip J.R. Goulder[1,2], and Christian Brander[1]

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The HIV Immunology database at the Los Alamos National Laboratory has collected data on HIV-specific cellular immune responses for over 8 years now and the list of targeted regions within the HIV protein sequences has been growing steadily. These compiled data and our own studies using comprehensive sets of overlapping peptides indicate that almost all parts of the viral protein sequence can be targeted by virus-specific T cells, especially CTL [Addo2003, Frahm2003]. HIV is the pathogen that has been characterized most extensively in terms of T-cell epitope distribution and the well-defined epitope landscape of HIV has allowed for a number of studies beyond assessing CTL activity in relation to HIV disease progression [Brander2002].

Targets of HIV-specific CTL

Whilst in the early years of HIV CTL epitope mapping, attention was focused on structural proteins, more recent studies have included regulatory and accessory proteins as well [Tomiyama1999a, Altfeld2001a, van Baalen1997, Addo2001, Addo2002b]. High-throughput assays such as intracellular cytokine staining (ICS), and the Elispot assay are now routinely used to assess genome wide immune responses to HIV [Edwards2002, Frahm2003, Betts2001, Addo2003, Novitsky2001, Novitsky2002]. This is especially true for the characterization of CD8+ CTL responses, but newer data also include the identification of Th cell activity. Studies from several labs, including ours, using overlapping peptide sets spanning the entire HIV protein sequence have now shown that at least 90% of these peptides can be targeted by HIV-specific CTL, indicating that all viral proteins undergo appropriate antigen processing *in vivo* and that epitopes from all HIV proteins can be effectively presented to CD8 T cells [Addo2003, Frahm2003]. However, there are specific patterns among these responses which will impact HIV vaccine design and which can potentially help to address more fundamental aspects of antigen processing, antigen presentation and T-cell repertoire development [Yusim2002].

Of special interest for these extended studies, but also for questions of CTL escape and (sub-unit)-vaccine development, is the identification of optimally defined CTL epitopes. Since 1995, largely through the voluntary contributions of unpublished data from many laboratories, regularly updated lists of "optimal CTL epitopes" have been made accessible through the Los Alamos National Laboratory's HIV database [Brander1995]. This year's update again adds a number of new epitopes whilst some others were removed as they were erroneously included before (mainly some HLA-A*0201 restricted epitopes from our own lab which were based on epitope prediction only and which were not defined with the same stringency as the other epitopes in this list). While the earliest reports clearly focused on alleles common in individuals infected early in the US epidemic, more attention is now given to individuals of non-Caucasian descent [Frahm2003, Sabbaj2003]. In addition, epitopes from non-clade B infections are increasingly identified [Novitsky2002, Novitsky2003, Bond2001, Fukada2002, Lynch1998, Sriwanthana2001, Goulder2001]. The identification of these epitopes provides valuable information for vaccine development in non-Caucasians and non-clade B infection.

In addition, these new epitopes, when characterized in full detail, can provide important insights into HLA binding motifs for these less well characterized alleles; again facilitating the design of a potential HIV vaccine. To support this work, the HIV database offers additional tools such as
EPILIGN:
`http://hiv-web.lanl.gov/content/hiv-db/EPILIGN/EPI.html`,
PeptGen:
`http://hiv-web.lanl.gov/content/hiv-db/PEPTGEN/PeptGenSubmitForm.html`

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MotifScan:
`http://hiv-web.lanl.gov/content/hiv-db/MOTIFSCAN/MotifScanner.html`
as well as valuable links to other sites, including the
SYFPEITHI HLA binding motifs database:
`http://www.syfpeithi.de/`
and others:
`http://hiv.basic.nwu.edu/HLA`,
`http://bimas.dcrt.nih.gov/cgi-bin/molbio/ken_parker_comboform`,
`http://www.jenner.ac.uk/JenPep/`
Clearly, these databases and prediction softwares can profit from each other and facilitate the future identification of T-cell targets in HIV and other infections.

Immunodominant regions in HIV protein sequences

As mentioned above, the described optimal CTL epitopes are not evenly distributed over the entire viral genome. Rather, there are regions where many epitopes overlap. This phenomenon has been described as early as 1993 and various explanations have been put forward [Goulder2000a, Buseyne1993]. Two factors that seem to significantly contribute to this epitope clustering appear to be viral sequence heterogeneity and processing preferences [Yusim2002].

Sequence heterogeneity affects all HIV proteins, albeit to variable degrees. Relatively conserved regions in Gag and Nef have been identified as immunodominant regions in a study of more than 150 individuals of different ethnicities [Frahm2003]. Independently of the HLA background, these clade B infected individuals made strong responses to the peptides spanning these regions. When comparing the sequence heterogeneity in published clade B sequences, these data also show that peptides with low sequence entropy (more conserved) are targeted more frequently than epitopes with higher entropy. It is likely that these differences are due to the fact that the average phylogenetic distance of the test reagent (consensus B sequence) to an individual‘s autologous viral sequence is larger in higher variable regions than in more conserved ones and thus, responses against the less conserved peptides are not detected due to differences between test reagent and inoculum sequence [Yusim2002, Gaschen2002].

In addition to sequence incompatibility between test reagent and autologous virus, certain regions of the HIV protein sequence may not be processed and presented very effectively. Although 86% of our overlapping peptide sets used in the study above were targeted by at least one individual in the cohort of 150 people, there are still some relatively conserved peptides that do not seem to induce a detectable CTL response in natural HIV infection [Frahm2003]. These peptides may lie within stretches of viral proteins that are relatively resistant to proteasomal digestions or may lack adequate “Transporter associated with Antigen Processing” (TAP) binding motifs [Brander2002, Yusim2002]. The HIV Immunology database provides valuable web links to software where sequences of choice can be analyzed for proteasomal processing preferences (NetChop by C. Kesmir *et al.*, `http://www.cbs.dtu.dk/services/NetChop/`). Recent work by Yusim *et al.*, demonstrates the accuracy and predictive potential of this algorithm and its usefulness in identifying CTL epitopes [Yusim2002].

Together, these studies indicate that CTL epitope clustering may reflect the biased detection of these responses in rather conserved regions and that processing preferences may play an important role in providing processed antigen. In addition, sequence variability may not only affect CTL recognition but could also have an effect on processing of viral proteins [Yellen-Shaw1997]. Although we have been unable to show such an effect for the flanking regions of the immunodominant, HLA-A*0201 restricted CTL epitope SL9 (SLYNTVATL) in HIV Gag p17, other studies outside the HIV field suggest that escape from processing may be an effective means of immune evasion [Yellen-Shaw1997, Kuckelkorn2002, Gileadi1999, Brander1999]. These studies also highlight the importance of defining T-cell targets in maximal detail, so that prediction algorithm such as NetChop and binding motif algorithms can be optimized by a precisely characterized training set of defined epitopes. In addition, in order to discriminate between processing escape and escape from T-cell receptor recognition or HLA binding, the boundaries of targeted epitopes need to be optimally determined. The present listing is designed to provide these data specifically for HIV derived epitopes and we therefore still separate CTL epitopes in a list of optimally and suboptimally defined epitopes. We hope that this discrimination continues to provide support for the HIV immunologists and laboratories involved in antigen processing and presentation, who want to take advantage of the exceptionally well defined epitope landscape of HIV.

As every year, we would like to express our gratitude to the large number of researchers in the field who continuously contribute to this database. We very much welcome any criticism, comments and additions to this list since we are sure that some epitopes will unintentionally escape our attention, despite close monitoring of the literature. Also, pertinent information, such as resources for single HLA allele expressing cell lines, HLA subtype information and new technologies for CTL epitope mapping could be listed or referenced in this list, providing additional help to problems encountered by investigators.

Optimal HIV-1 CTL Epitopes

Acknowledgments

The mostly unpublished data added to this years update stemming from the AIDS Research Center at Massachussetts General Hospital have been largely funded by an NIH contract (#NO1-A1-15442) supporting HLA typing and HIV CTL epitope definition in non-Caucasian populations and non-clade B HIV infection.

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Optimal HIV-1 CTL Epitopes

Table 1: Best Defined HIV CTL Epitopes

HLA	Protein	AA	Sequence	Reference
A*0101 (A1)	gp160	787–795	RRGWEVLKY	[Cao2002]
A*0201 (A2)			2 6 C	[Falk1991, Barouch1995]
		1° anchor	**L** **L**	
			M **V**	
		2° anchor	V	
A*0201 (A2)	p17	77–85	SLYNTVATL	[Johnson1991, Parker1992, Parker1994]
A*0201 (A2)	p1	1–10	FLGKIWPSYK	[Yu2002b]
A*0201 (A2)	RT	33–41	ALVEICTEM	[Haas1998, Haas1999]
A*0201 (A2)	RT	179–187	VIYQYMDDL	[Harrer1996a]
A*0201 (A2)	RT	309–317	ILKEPVHGV	[Walker1989, Tsomides1991]
A*0201 (A2)	Vpr	59–67	AIIRILQQL	[Altfeld2001a, Altfeld2001b]
A*0201 (A2)	gp160	311–320	RGPGRAFVTI	[Alexander-Miller1996]
A*0201 (A2)	gp160	813–822	SLLNATDIAV	[Dupuis1995]
A*0201 (A2)	Nef	136–145	PLTFGWCYKL	[Haas1996, Maier1999]
A*0201 (A2)	Nef	180–189	VLEWRFDSRL	[Haas1996, Maier1999]
A*0202 (A2)			2 C	[Barouch1995]
			L **L**	
			V	
A*0202 (A2)	p17	77–85	SLYNTVATL	[Goulder1999]
A*0205 (A2)	p17	77–85	SLYNTVATL	[Goulder1999]
A*0205 (A2)	gp41	335–343	RIRQGLERA	[Sabbaj2003]
A*0207 (A2)	p24	164–172	YVDRFYKTL	[Currier2002]
A*03 (A3)	RT	73–82	KLVDFRELNK	[Yu2002a]
A*03 (A3)	RT	356–366	RMRGAHTNDVK	[Yu2002a]
A*03 (A3)	Integrase	179–188	AVFIHNFKRK	[Yu2002a]
A*03 (A3)	Vif	28–36	HMYISKKAK	[Yu2002a]
A*03 (A3)	Vif	158–168	KTKPPLPSVKK	[Yu2002a]
A*03 (A3)	Rev	57–66	ERILSTYLGR	[Addo2002a, Yu2002a]
A*03 (A3)	Nef	84–92	AVDLSHFLK	[Yu2002a]

Optimal HIV-1 CTL Epitopes

Table 1 (cont.): Best Defined HIV CTL Epitopes

HLA	Protein	AA	Sequence	Reference
A*0301 (A3)			2 C	[DiBrino1993, Rammensee1995]
			L K	
			V Y	
			M F	
A*0301 (A3)	p17	18–26	KIRLRPGGK	[Harrer1996b]
A*0301 (A3)	p17	20–28	RLRPGGKKK	[Goulder1997a, Culmann1999, Lewinsohn1999b, Wilkes1999b]
A*0301 (A3)	p17	20–29	RLRPGGKKKY	[Goulder2000b]
A*0301 (A3)	RT	33–43	ALVEICTEMEK	[Haas1998, Haas1999]
A*0301 (A3)	RT	93–101	GIPHPAGLK	[Yu2002a]
A*0301 (A3)	RT	158–166	AIFQSSMTK	[Threlkeld1997]
A*0301 (A3)	RT	269–277	QIYPGIKVR	[Yu2002a]
A*0301 (A3)	Vif	17–26	RIRTWKSLVK	[Altfeld2001a, Yu2002a]
A*0301 (A3)	gp160	37–46	TVYYGVPVWK	[Johnson1994a]
A*0301 (A3)	gp160	770–780	RLRDLLLIVTR	[Takahashi1991]
A*0301 (A3)	Nef	73–82	QVPLRPMTYK	[Koenig1990, Culmann1991]
A*1101 (A11)			2 C	[Zhang1993, Rammensee1995]
			K	
			V	
			I	
			F	
			Y	
A*1101 (A11)	p17	84–92	TLYCVHQRI	[Harrer1998]
A*1101 (A11)	p24	217–227	ACQGVGGPGHK	[Sipsas1997]
A*1101 (A11)	RT	158–166	AIFQSSMTK	[Johnson1994b, Zhang1993, Threlkeld1997]
A*1101 (A11)	RT	341–350	IYQEPFKNLK	[Culmann1999]
A*1101 (A11)	RNase	80–88	QIIEQLIKK	[Fukada1999]
A*1101 (A11)	Integrase	179–188	AVFIHNFKRK	[Fukada1999]
A*1101 (A11)	gp160	199–207	SVITQACPK	[Fukada1999]
A*1101 (A11)	Nef	73–82	QVPLRPMTYK	[Buseyne1999]
A*1101 (A11)	Nef	75–82	PLRPMTYK	[Culmann1991]
A*1101 (A11)	Nef	84–92	AVDLSHFLK	[Culmann1991]
A*23 (A23)	gp41	74–82	RYLKDQQLL	[Cao2003]

Optimal HIV-1 CTL Epitopes

Table 1 (cont.): Best Defined HIV CTL Epitopes

HLA	Protein	AA	Sequence	Reference
A*2402 (A24)			2 C **Y** **I** **L** **F**	[Maier1994]
A*2402 (A24)	p17	28–36	KYKLKHIVW	[Ikeda-Moore1998, Lewinsohn1999a]
A*2402 (A24)	p24	162–172	RDYVDRFFKTL	[Dorrell1999, Rowland-Jones1999]
A*2402 (A24)	gp160	52–61	LFCASDAKAY	[Lieberman1992, Shankar1996]
A*2402 (A24)	gp160	585–593	RYLKDQQLL	[Dai1992]
A*2402 (A24)	Nef	134–141	RYPLTFGW	[Goulder1997b, Ikeda-Moore1998]
A*2501 (A25)	p24	13–23	QAISPRTLNAW	[Kurane1999]
A*2501 (A25)	p24	71–80	ETINEEAAEW	[Klenerman1996, van Baalen1996]
A*2601 (A26)			12 6 C **V** **Y** **T** **F** **I** **L** **F** D I E L V	[Dumrese1998]
A*2601 (A26)	p24	35–43	EVIPMFSAL	[Goulder1996a]
A*2601 (A26)	Pol	604–612	ETKLGKAGY	[Sabbaj2003]
A*2902 (A29)	gp160	209–217	SFEPIPIHY	[Altfeld2000a]

Optimal HIV-1 CTL Epitopes

Table 1 (cont.): Best Defined HIV CTL Epitopes

HLA	Protein	AA	Sequence	Reference
A*3002 (A30)			12 C **Y** **Y** **F** **L** **V** R	[Rammensee1999]
A*3002 (A30)	p17	76–86	RSLYNTVATLY	[Goulder2001]
A*3002 (A30)	RT	173–181	KQNPDIVIY	[Goulder2001]
A*3002 (A30)	RT	263–271	KLNWASQIY	[Goulder2001]
A*3002 (A30)	RT	356–365	RMRGAHTNDV	[Sabbaj2003]
A*3002 (A30)	Integrase	219–227	KIQNFRVYY	[Sabbaj2003, Addo2002c]
A*3002 (A30)	gp160	704–712	IVNRNRQGY	[Goulder2001]
A*3002 (A30)	gp120	310–318	HIGPGRAFY	[Sabbaj2003]
A*3002 (A30)	gp41	283–291	KYCWNLLQY	[Goulder2001]
A*3101 (A31)			2 C **R** L V Y F	[Falk1994, Rammensee1999]
A*3101 (A31)	gp160	770–780	RLRDLLLIVTR	[Safrit1994a, Safrit1994b]
A*3201 (A32)	RT	392–401	PIQKETWETW	[Harrer1996b]
A*3201 (A32)	gp160	419–427	RIKQIINMW	[Harrer1996b]
A*3303 (A33)	gp41	187–196	VFAVLSIVNR	[Hossain2001]
A*3303 (A33)	gp41	320–327	EVAQRAYR	[Hossain2001]
A*3303 (A33)	Vpu	29–37	EYRKILRQR	[Addo2002b]
A*3303 (A33)	Nef	133–141	TRYPLTFGW	[Cao2002]
A*6801 (A68)	Tat	39–49	ITKGLGISYGR	[Oxenius2002]
A*6802 (A68)	Protease	3–11	ITLWQRPLV	[Rowland-Jones1999]
A*6802 (A68)	Protease	30–38	DTVLEEWNL	[Rowland-Jones1999]
A*6802 (A68)	gp160	777–785	IVTRIVELL	[Wilkes1999a]
A*7401 (A19)	Protease	3–11	ITLWQRPLV	[Rowland-Jones1999]

Optimal HIV-1 CTL Epitopes

Table 1 (cont.): Best Defined HIV CTL Epitopes

HLA	Protein	AA	Sequence	Reference
B*07 (B7)	p24	84–92	HPVHAGPIA	[Yu2002a]
B*0702 (B7)			123 C **P L** A R R K	[Englehard1993, Rammensee1999]
B*0702 (B7)	p24	16–24	SPRTLNAWV	[Lewinsohn1999a]
B*0702 (B7)	p24	48–56	TPQDLNTML	[Wilson1999a, Wilkes1999c, Jin2000, Wilson1997]
B*0702 (B7)	p24	223–231	GPGHKARVL	[Goulder1999]
B*0702 (B7)	Vpr	34–42	FPRIWLHGL	[Altfeld2001a]
B*0702 (B7)	Vif	48–57	HPRVSSEVHI	[Altfeld2001a]
B*0702 (B7)	gp160	298–307	RPNNNTRKSI	[Safrit1994b]
B*0702 (B7)	gp160	843–851	IPRRIRQGL	[Wilkes1999b]
B*0702 (B7)	Nef	68–77	FPVTPQVPLR	[Haas1996, Maier1999]
B*0702 (B7)	Nef	68–76	FPVTPQVPL	[Bauer1997, Frahm2002]
B*0702 (B7)	Nef	71–79	TPQVPLRPM	[Goulder1999]
B*0702 (B7)	Nef	77–85	RPMTYKAAL	[Bauer1997]
B*0702 (B7)	Nef	106–115	RQDILDLWIY	[Goulder1999]
B*0702 (B7)	Nef	128–137	TPGPGVRYPL	[Culmann-Penciolelli1994, Haas1996]
B*0801 (B8)			23 5 C **K K L** **R** PR L	[Hill1992, Sutton1993, DiBrino1994a]
B*0801 (B8)	p17	24–32	GGKKKYKLK	[Rowland-Jones1993, Goulder1997d]
B*0801 (B8)	p17	74–82	ELRSLYNTV	[Goulder1997d]
B*0801 (B8)	p24	128–135	EIYKRWII	[Sutton1993, Goulder1997d]
B*0801 (B8)	p24	197–205	DCKTILKAL	[Sutton1993]
B*0801 (B8)	RT	18–26	GPKVKQWPL	[Walker1989, Sutton1993]
B*0801 (B8)	gp160	2–10	RVKEKYQHL	[Sipsas1997]
B*0801 (B8)	gp160	586–593	YLKDQQLL	[Johnson1992, Shankar1996]
B*0801 (B8)	Nef	13–20	WPTVRERM	[Goulder1997d]
B*0801 (B8)	Nef	90–97	FLKEKGGL	[Culmann-Penciolelli1994, Price1997]
B*14 (B14)	p15	42–50	CRAPRKKGC	[Yu2002b]

Optimal HIV-1 CTL Epitopes

Table 1 (cont.): Best Defined HIV CTL Epitopes

HLA	Protein	AA	Sequence	Reference
B*1402 (B14)			23 5 C	[DiBrino1994b]
			R R L	
			K H	
			L	
			Y	
			F	
B*1402 (B14)	p24	166–174	DRFYKTLRA	[Harrer1996b]
B*1402 (B14)	gp160	584–592	ERYLKDQQL	[Johnson1992]
B*1501 (B62)			2 C	
			Q Y	[Barber1997]
			L F	[Barber1997]
			M	[Barber1997]
B*1501 (B62)	p24	137–145	GLNKIVRMY	[Johnson1991, Goulder1999]
B*1501 (B62)	RT	260–271	LVGKLNWASQIY	[Johnson1999]
B*1501 (B62)	RT	309–318	ILKEPVHGVY	[Johnson1991, Johnson1999]
B*1501 (B62)	Nef	19–27	RMRRAEPAA	[Cao2002]
B*1501 (B62)	Nef	117–127	TQGYFPDWQNY	[Culmann1999]
B*1503 (B72)	Integrase	263–271	RKAKIIRDY	[Cao2003]
B*1503 (B72)	Tat	38–47	FQTKGLGISY	[Novitsky2001]
B*1503 (B72)	Pol	651–660	VTDSQYALGI	[Sabbaj2003]
B*1503 (B72)	Nef	183–191	WRFDSRLAF	[Cao2002]
B*1516 (B63)			2 9	[Barber1997, Seeger1998]
			T Y	
			S I	
			V	
			F	
B*1516 (B63)	gp160	375–383	SFNCGGEFF	[Wilson1997, Wilson1999a]
B*1801 (B18)	p24	161–170	FRDYVDRFYK	[Ogg1998]
B*1801 (B18)	Vif	102–111	LADQLIHLHY	[Altfeld2001a]
B*1801 (B18)	Nef	135–143	YPLTFGWCY	[Culmann1991, Culmann-Penciolelli1994]
B*2703 (B27)	p24	131–140	RRWIQLGLQK	[Rowland-Jones1998, Rowland-Jones1999]

Optimal HIV-1 CTL Epitopes

Table 1 (cont.): Best Defined HIV CTL Epitopes

HLA	Protein	AA	Sequence	Reference
B*2705 (B27)			12 C **R** **L** **F** K K R R G I A	[Jardetzky1991, Rammensee1995]
B*2705 (B27)	p17	19–27	IRLRPGGKK	[McKinney1999, Lewinsohn1999a]
B*2705 (B27)	p24	131–140	KRWIILGLNK	[Nixon1988, Buseyne1993, Goulder1997c]
B*2705 (B27)	gp160	786–795	GRRGWEALKY	[Lieberman1992, Lieberman1999]
B*2705 (B27)	Nef	105–114	RRQDILDLWI	[Goulder1997a]
B*3501 (B35)			2 C **P** **Y** A F V M S L I	[Hill1992, Rammensee1999]
B*3501 (B35)	p17	36–44	WASRELERF	[Goulder1997b]
B*3501 (B35)	p17	124–132	NSSKVSQNY	[Rowland-Jones1995]
B*3501 (B35)	p24	122–130	PPIPVGDIY	[Rowland-Jones1995]
B*3501 (B35)	p24	122–130	NPVPVGNIY	[Rowland-Jones1995]
B*3501 (B35)	RT	107–115	TVLDVGDAY	[Wilkes1999b, Wilson1999b]
B*3501 (B35)	RT	118–127	VPLDEDFRKY	[Sipsas1997, Shiga1996]
B*3501 (B35)	RT	175–183	NPDIVIYQY	[Sipsas1997, Shiga1996]
B*3501 (B35)	RT	175–183	HPDIVIYQY	[Rowland-Jones1995]
B*3501 (B35)	gp160	42–52	VPVWKEATTTL	[Wilkes1999b]
B*3501 (B35)	gp160	78–86	DPNPQEVVL	[Shiga1996]
B*3501 (B35)	gp160	606–614	TAVPWNASW	[Johnson1994a]
B*3501 (B35)	Nef	74–81	VPLRPMTY	[Culmann1991, Culmann-Penciolelli1994]
B*3701 (B37)			2 C **D** **F** **E** **M** **L** **I**	[Falk1993]
B*3701 (B37)	Nef	120–128	YFPDWQNYT	[Culmann1991, Culmann1999]

Optimal HIV-1 CTL Epitopes

Table 1 (cont.): Best Defined HIV CTL Epitopes

HLA	Protein	AA	Sequence	Reference
B*3801 (B38)	gp160	104–112	MHEDIISLW	[Cao2002]
B*3901 (B39)			2 C **R L** **H**	[Falk1995a]
B*3901 (B39)	p24	61–69	GHQAAMQML	[Kurane1999]
B*4001 (B60)			2 C **E L**	[Falk1995b]
B*4001 (B60)	p17	92–101	IEIKDTKEAL	[Altfeld2000b]
B*4001 (B60)	p24	44–52	SEGATPQDL	[Altfeld2000b]
B*4001 (B60)	p6	33–41	KELYPLTSL	[Yu2002b]
B*4001 (B60)	RT	202–210	IEELRQHLL	[Altfeld2000b]
B*4001 (B60)	gp160	805–814	QELKNSAVSL	[Altfeld2000b]
B*4001 (B60)	Nef	92–100	KEKGGLEGL	[Altfeld2000b]
B*4002 (B61)	p17	11–19	GELDRWEKI	[Sabbaj2003]
B*4002 (B61)	p24	70–78	KETINEEAA	[Sabbaj2003]
B*4002 (B61)	p24	78–86	AEWDRVHPV	[Sabbaj2003]
B*4002 (B61)	Nef	92–100	KEKGGLEGL	[Sabbaj2003, Altfeld2000b]
B*4002 (B61)	p15	64–71	TERQANFL	[Sabbaj2003]
B*42 (B42)	Integrase	260–268	VPRRKAKII	[Kiepiela2002]
B*4201 (B42)	p24	48–56	TPQDLNTML	[Goulder2000a]
B*4201 (B42)	RT	271–279	YPGIKVRQL	[Wilkes1999b]
B*4201 (B42)	Nef	128–137	TPGPGVRYPL	[Goulder1999]
B*4402 (B44)			2 C **E F** **Y**	[Rammensee1999]
B*4402 (B44)	p24	162–172	RDYVDRFYKTL	[Ogg1998]
B*4402 (B44)	p24	174–184	AEQASQDVKNW	[Lewinsohn1999a]
B*4402 (B44)	gp160	31–40	AENLWVTVYY	[Borrow1997]
B*4415 (B12)	p24	28–36	EEKAFSPEV	[Bird2002]
B*51 (B51)	Vpr	29–37	EAVRHFPRI	[Cao2003]

Optimal HIV-1 CTL Epitopes

Table 1 (cont.): Best Defined HIV CTL Epitopes

HLA	Protein	AA	Sequence	Reference
B*5101 (B51)			2 C **A F** **P I** **G**	[Falk1995a]
B*5101 (B51)	RT	42–50	EKEGKISKI	[Haas1998, Haas1999]
B*5101 (B51)	RT	128–135	TAFTIPSI	[Sipsas1997]
B*5101 (B51)	gp160	416–424	LPCRIKQII	[Tomiyama1999b]
B*5201 (B52)			2 C **I** **V** Q	[Rammensee1999]
B*5201 (B52)	p24	143–150	RMYSPTSI	[Wilkes1999b, Wilson1997]
B*53 (B53)	Nef	135–143	YPLTFGWCF	[Kiepiela2002]
B*5301 (B53)			2 C **P L**	[Hill1992]
B*5301 (B53)	p24	48–56	TPYDINQML	[Gotch1993]
B*5301 (B53)	p24	176–184	QASQEVKNW	[Buseyne1996, Buseyne1997, Buseyne1999]
B*5301 (B53)	Tat	2–11	EPVDPRLEPW	[Addo2001]
B*5301 (B53)	Nef	135–143	YPLTFGWCY	[Sabbaj2003]
B*5501 (B55)			2 C **P** A	[Barber1995]
B*5501 (B55)	gp160	42–51	VPVWKEATTT	[Shankar1996, Lieberman1999]

Optimal HIV-1 CTL Epitopes

Table 1 (cont.): Best Defined HIV CTL Epitopes

HLA	Protein	AA	Sequence	Reference
B*5701 (B57)			12 C **A F** **T W** **S** K Y	[Barber1997]
B*5701 (B57)	p24	15–23	ISPRTLNAW	[Johnson1991, Goulder1996b]
B*5701 (B57)	p24	30–40	KAFSPEVIPMF	[Goulder1996b]
B*5701 (B57)	p24	108–118	TSTLQEQIGWF	[Goulder1996b]
B*5701 (B57)	p24	176–184	QASQEVKNW	[Goulder1996b]
B*5701 (B57)	RT	244–252	IVLPEKDSW	[van der Burg1997, Hay1999]
B*5701 (B57)	Integrase	173–181	KTAVQMAVF	[Goulder1996b, Hay1999]
B*5701 (B57)	Vpr	30–38	AVRHFPRIW	[Altfeld2001a]
B*5701 (B57)	Vif	31–39	ISKKAKGWF	[Altfeld2001a]
B*5701 (B57)	Rev	14–23	KAVRLIKFLY	[Addo2001]
B*5701 (B57)	Nef	116–125	HTQGYFPDWQ	[Culmann1991]
B*5701 (B57)	Nef	120–128	YFPDWQNYT	[Culmann1991]
B57 (B57)	Nef	116–124	HTQGYFPDW	[Draenert2002]
B*5703 (B57)	p24	30–37	KAFSPEVI	[Goulder2000b]
B*5703 (B57)	p24	30–40	KAFSPEVIPMF	[Goulder2000b]
B*5801 (B58)			12 C **A F** **T W** **S** K V I	[Barber1997, Falk1995b]
B*5801 (B58)	p24	108–117	TSTVEEQQIW	[Bertoletti1998]
B*5801 (B58)	p24	108–117	TSTLQEQIGW	[Goulder1996b]
B*5801 (B58)	RT	375–383	IAMESIVIW	[Kiepiela2002]
B*5801 (B58)	Rev	14–23	KAVRLIKFLY	[Addo2001]
B*81 (B81)	Pol	715–723	LFLDGIDKA	[Addo2002a]

Optimal HIV-1 CTL Epitopes

Table 1 (cont.): Best Defined HIV CTL Epitopes

HLA	Protein	AA	Sequence	Reference
B*8101 (B81)	p24	48–56	TPQDLNTML	[Goulder2000a]
B*8101 (B81)	Vpr	34–42	FPRIWLHGL	[Altfeld2001a]
Cw*0102 (Cw1)			23 C **A** **L** **L** P	[Barber1997]
Cw*0102 (Cw1)	p24	36–43	VIPMFSAL	[Goulder1997b]
Cw*0304 (Cw10)	gp41	46–54	RAIEAQQHL	[Currier2002, Trocha2002]
Cw*0401 (Cw4)			2 6 C **Y** **L** **P** **F** **F** **M** V I L	[Falk1994]
Cw*0401 (Cw4)	gp160	375–383	SFNCGGEFF	[Wilson1997, Johnson1993]
Cw*0501 (Cw5)	Rev	67–75	SAEPVPLQL	[Addo2001]
Cw*07 (Cw7)	Nef	105–115	KRQEILDLWVY	[Kiepiela2002]
Cw*07 (Cw7)	Nef	105–115	RRQDILDLWIY	[Yu2002a]
Cw*0802 (Cw8)	p24	48–56	TPQDLNTML	[Goulder2000a]
Cw*0802 (Cw8)	Nef	83–91	AAVDLSHFL	[Cao2003]
Cw*12 (Cw12)	Tat	30–37	CCFHCQVC	[Cao2003, Nixon1999]
Cw*15 (Cw15)	gp41	46–54	RAIEAQQHL	[Trocha2002]

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Mutational Analyses and Natural Variability of the gp41 Ectodomain

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The HIV-1 envelope glycoproteins mediate viral attachment and release of the viral core in susceptible target cells. A single gp160 precursor protein is processed intracellularly to yield the native form of the envelope complex, consisting of three gp120 and three gp41 molecules associated through non-covalent interactions. Upon receptor and co-receptor binding to the surface subunit gp120, conformational changes within the envelope glycoprotein complex enable the insertion of the hydrophobic fusion peptide of the transmembrane subunit gp41 into the target membrane. Subsequent rearrangements within gp41 allow fusion of viral and cellular membranes. These late structural alterations are targeted by the entry inhibitor T-20 (for reviews see 13, 20, 21, 24, 46, 75).

A considerable body of mutagenesis data on structure-function relationships within the HIV-1 gp41 ectodomain (gp41e) has been published over the years. The value of this data-set has been increased considerably by the determination of the structure of the gp41e core, allowing some of the mutational effects to be interpreted and at least partially understood (9, 12, 38, 41, 68, 71). The native, pre-fusion structure of gp41e in the trimeric gp120-gp41 complex on the virion surface prior to receptor engagement is not known, however, and the various transitional structures of gp41 during the virus-cell fusion process are still ill-defined. Consequently, the structural and functional consequences of many amino acid substitutions in gp41e remain unclear.

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Here, we have summarized the results of published mutagenesis studies on gp41e (see the accompanying table). The HXB2 reference strain has been used as a basis for numbering individual amino acid residues (Figure 1). This information should facilitate the research of those who study the HIV-1 envelope glycoproteins as fusogens or vaccine antigens. In general, we have tabulated only data for single mutants, but several publications contain information on the effects of multiple amino acid substitutions (25, 43, 44, 49, 56, 57, 62). The table does not include information on every naturally occurring gp41e sequence variant, as the variation is extensive. However, a summary of natural variability in clades B and C is presented in Figure 2. Also, the last two columns in the table present the entropy scores for gp41e positions that have a defined impact on Env function, for both the B clade and the C clade. Not surprisingly, positions identified through mutational analysis as those where substitutions can abrogate key functions, also tend to be highly conserved among the natural variants. The clearest example is provided by positions where substitutions essentially eliminate cell-cell fusion (*i.e.*, where fusion efficiencies in syncytium assays or reporter gene assays have been reduced to less than 3% of the wild-type value). Sites at which substitutions can abrogate cell-cell fusion tended to be more invariant among 123 B clade sequences (26/44, 59%), compared to those sites where amino acid changes did not dramatically reduce fusion (11/39, 28%, Fisher's exact test $p = 0.004$). Some unusual gp41e variants found in neutralization-resistant isolates are also included in the table, as are variants that arise in response to selection pressure, both *in vitro* and *in vivo*, from the entry inhibitor T-20, which targets gp41e.

The precision with which the available data could be analyzed was sometimes limited because different viral clones, isolates and assays were used to obtain the experimental data. We have therefore chosen to summarize quantitative parameters using the grading system –, +, ++ and +++, as indicated in the footnotes. In some cases these grades had to be deduced from the primary reports, so readers are encouraged to consult the original papers for quantitative details; we regret any errors of interpretation we may have made during this estimation process. Not surprisingly, perhaps, different studies sometimes yielded conflicting results. We have recorded the conflicting data sets but shall leave it to the readers to judge which are the more plausible.

The natural variability of residues in clade B and C isolates was analyzed and mapped on the structure of gp41 (see Figures 2 and 3). A focus of variable residues in clade B sequences is located in the upper part of the C-terminal helix

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centered around the highly variable leucine-glutamate-glutamine (LEQ) triplet, indicating that this region is under selective pressure. However, it is also possible that certain changes in residues in this region have little impact on Env function, particularly if there is some flexibility in Env structure(s) around this region. This relatively variable region also contains four glycosylation sites, which could be involved in immune evasion (30). Indeed, mutations that affect glycosylation in this region can modulate neutralization sensitivity (65). Of note is that no CTL or antibody epitopes have been mapped to this region despite the intense positive selection. One interpretation of this observation is that the selection pressure is exerted indirectly on distant antibody epitopes elsewhere in gp41e or even in gp120 (32). Another is that some neutralizing antibodies remain as yet undiscovered in this region of gp41e. In clade C viruses the variability is somewhat shifted towards the 2F5 epitope, compared to clade B. Furthermore, certain residues are significantly more variable in clade C viruses compared to clade B, and vice versa, suggesting that subtly different selection pressures may operate on viruses from the two clades.

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gp41 start, position 512 of HXB2 gp160

```
                |
          AVGIGALFL GFLGAAGSTM GAASMTLTVQ ARQLLSGIVQ  550
QQNNLLRAIE AQQHLLQLTV WGIKQLQARI LAVERYLKDQ QLLGIWGCSG  600
KLICTTAVPW NASWSNKSLE QIWNHTTWME WDREINNYTS LIHSLIEESQ  650
NQQEKNEQEL LELDKWASLW NWFNITNWLW YIKLFIMIVG GLVGLRIVFA  700
VLSIVNRVRQ GYSPLSFQTH LPTPRGPDRP EGIEEEGGER DRDRSIRLVN  750
GSLALIWDDL RSLCLFSYHR LRDLLLIVTR IVELLGRRGW EALKYWWNLL  800
QYWSQELKNS AVSLLNATAI AVAEGTDRVI EVVQGACRAI RHIPRRIRQG  850
LERILL                                                  856
```

Figure 1: The HXB2 reference strain and the numbering of positions in the gp41 sequence. Only information on the ectodomain (residue 512–684) is incorporated in subsequent analyses.

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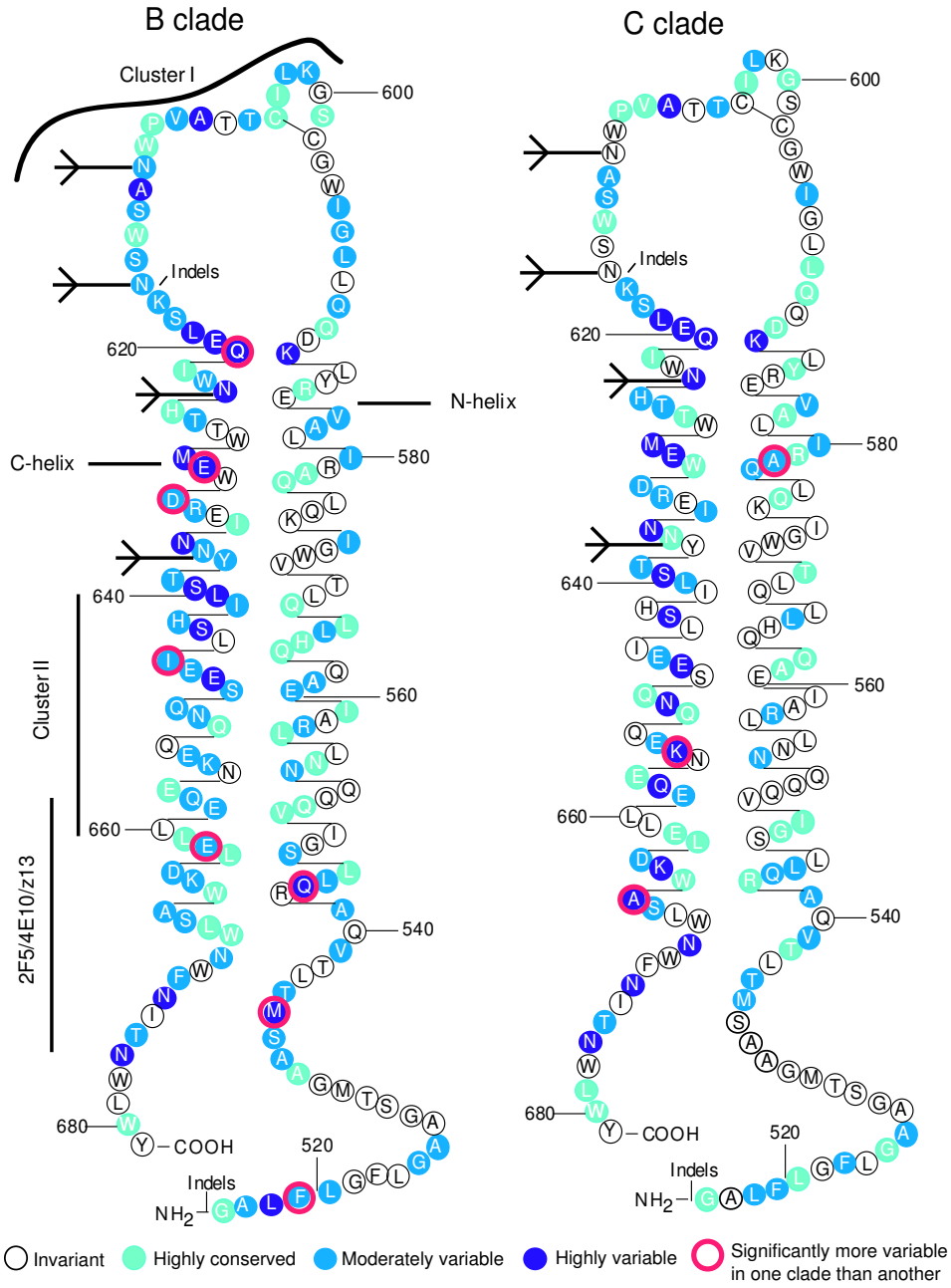

Figure 2: Variability of gp41e. The relative entropies of residues were mapped onto a 2D representation of the HXB2 gp41e (adapted from 29, 61). The variability of residues in clade B isolates (left panel) and clade C isolates (right panel) is indicated according to their entropy values. The entropy is a simple measure of variation in each position based on a sequence alignment (33). Not surprisingly, entropy values for each amino acid were highly correlated with the ratio of the nonsynonymous/synonymous substitution rates, a measure which is indicative of selective pressure, calculated using PAML (76) (Spearman's rank correlation tests gave $z = 7.3, p = 2 \times 10^{-13}$ for the B clade, and $z = 7.5, p = 5 \times 10^{-14}$ for the C clade). We used the entropy scores as our measure of variability here because they lent themselves to testing for differences in variability between the B clade and C clade (33). The color coding for the sites is as follows: white, invariant (entropy score of zero); light blue, very conserved (entropy score below the median, corresponding to only one observed substitution); medium blue, variable (entropy score above the median: 2 or more observed substitutions); dark blue, highly variable (highest 10% of entropy scores: > 0.8 for clade B and > 0.75 for clade C). Residues that are significantly more variable in clade B than in clade C or vice versa (p value ≤ 0.03 after a Bonferroni correction for multiple tests, using a Monte Carlo scheme and randomizing the B and C clade data 10,000 times) are indicated by red circles. 123 clade B sequences and 48 clade C sequences were used for the analyses. The four glycans and the major antibody epitopes (non-neutralizing clusters I and II and the neutralizing 2F5/4E10/z13 cluster) are also indicated, as are regions labelled "indel" where insertions and deletions are frequently observed in natural variants.

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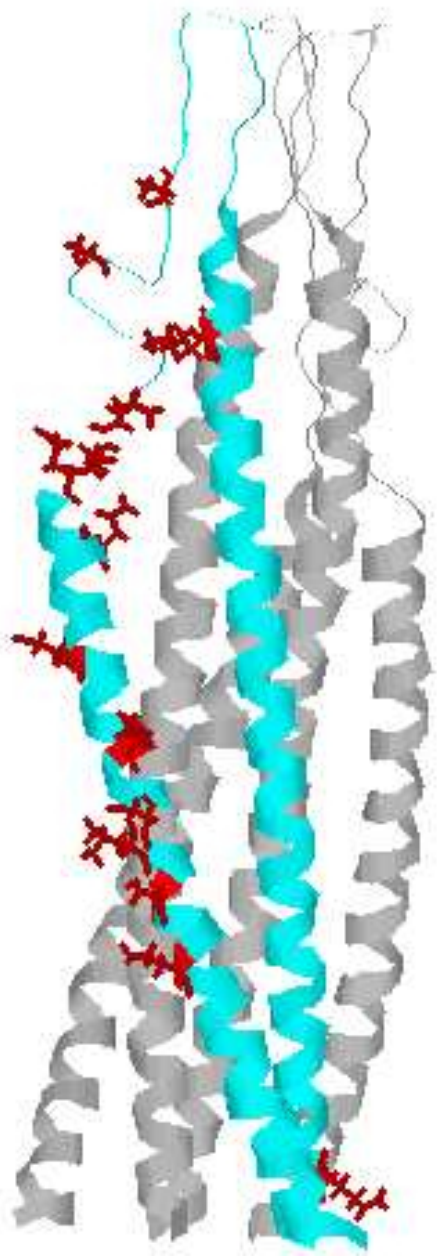

Figure 3: The residues with the highest 10% of entropy scores in clade B are indicated in red on the 3D structure model of Caffrey (pdb accession number 1IF3, (8)). These residues are only indicated in one monomer. The other two monomers are shown in grey for orientation purposes.

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Residue[1]	Comments	Substitution	Isolate[2]	Reference	Expression (cell lysate)[3]	Expression (cell surface)[4]	gp160 processing[5]	gp120 association[6]	CD4-binding[7]	CD4-induced shedding[8]	Cell-cell fusion[9]	Virion incorporation[10]	Virus entry[11]	Viral Replication[12]	Oligomerization (gp160/gp140)[13]	Trimerization (SOS gp140)[14]	Thermal stability (gp41 core)[15]	B-clade entropy	C-clade entropy
WT					++	++	++	++	++	++		++	++	++	++	+	++		
A512		V[16]	NL4-3	Freed90	++		++	++	++		+							0.136	0
		E	NL4-3	Freed90	++		++	++	++		+								
V513		E	NL4-3	Freed90	++		++	++	++		–							0.326	0.44
		A	NL4-3	Buchschacher95							++								
		G	NL4-3								++								
		R	NL4-3		++		++				–								
G514		V	NL4-3	Delahunty96	++		++	++			++							0.628	0.594
G516		V	NL4-3	Delahunty96	+++		++	++			++							0.047	0.101
A517		[17]	HXB2	Kowalski91	++	++	++	++	++					++				0.115	0
		[18]	HXB2	Kowalski91										–					
M518		V[19]	ELI1	Kozak97					+++					++				0.985	0.658
F519		L[16]	NL4-3	Freed90	++		++	++	++		+							0.19	0.473
		V	NL4-3	Delahunty96	+++		++	++			++			++					
L520		R	NL4-3	Freed90	++		++	++	++		–							0.13	0.101
G521		V	NL4-3	Delahunty96	+	++	++	++			–			–				0	0
F522		V	NL4-3	Delahunty96	+++		++	++			+							0	0.302
		G	BH8	Pritsker99	++		++				+								
G524		V	NL4-3	Delahunty96	+++	++	++	++			+			+				0.083	0.101
A525		T[20]	LAI	Bahbouhi01	++		++					++		++				0.115	0.202
A526		E	NL4-3	Freed90	++		+	+	++		–							0	0
G527		V	NL4-3	Delahunty96	+++		++	–			–							0	0
S528		T	HXB2	Cao93		+	+	–		+	–		+					0	0
M530		S	HXB2	Cao93		++	–	–		+	–		–					0	0
G531		V	NL4-3	Delahunty96	+++		++	++			++							0	0
L537		R	NL4-3	Freed90	++		+	+	++		–							0	0
V539		E	NL4-3	Freed90	++		++	++	++		+							0.083	0.334
Q540		L	NL4-3	Freed90	++		+	+	++		–							0	0
R542	e in heptad-repeat	G	NL4-3	Freed90	++		++	++	++		+							0	0.101
Q543	f in heptad-repeat	H	PI	Wei02, Kilby02										++				0.811	0.202
		R												++					
P543		L[28]	MN	Park00										++					
L544	g in heptad-repeat	S[22]	PI	Fikkert02										++				0.094	0.234

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Residue[1]	Comments	Substitution	Isolate[2]	Reference	Expression (cell lysate)[3]	Expression (cell surface)[4]	gp160 processing[5]	gp120 association[6]	CD4-binding[7]	CD4-induced shedding[8]	Cell-cell fusion[9]	Virion incorporation[10]	Virus entry[11]	Viral Replication[12]	Oligomerization (gp160/gp140)[13]	Trimerization (SOS gp140)[14]	Thermal stability (gp41 core)[15]	B-clade entropy	C-clade entropy
L545	a in heptad-repeat	F^{21}	JR-FL	Sanders02		–										+		0.047	0
		N^{21}	JR-FL			++										+			
		P^{21}	JR-FL			++										+			
		G^{21}	JR-FL			++										+			
G547	c in heptad-repeat	S^{22}	NL4-3	Rimsky98										++				0	0.101
		D^{22}	NL4-3											++					
		D^{22}	PI	Baldwin03										++					
		V^{22}	PI	Poveda02										++					
		D^{22}	PI	Wei02										++					
I548	d in heptad-repeat	A	HXB2	Cao93	++	++	+	+++		++	+		++					0	0.101
		T^{22}	NL4-3	Rimsky98										++					
		K^{22}	PI	Baldwin03										++					
		V^{22}	PI	Wei02, Kilby02										++					
		V^{21}	JR-FL	Sanders02		++										+			
		L^{21}	JR-FL			++										+			
		H^{21}	JR-FL			++										+			
		N^{21}	JR-FL			++										+			
		S^{21}	JR-FL			++										+			
		G^{21}	JR-FL			++										+			
		R^{21}	JR-FL			++										+			
V549	e in heptad-repeat	M^{22}	NL4-3	Rimsky98										++				0.047	0
		M^{22}	PI	Wei02										++					
		A^{22}	PI											++					
		A^{22}	PI	Baldwin03										++					
		W^{22}	PI											++					
		G^{22}	PI											++					
		A	HXB2	Lu01		++	++	++			++						++		
Q551	g in heptad-repeat	A	HXB2	Lu01, Follis02		++	++	++			++		++				++	0	0
Q552	a in heptad-repeat	L	HXB2	Cao93	++		–	–			–							0	0
N554	c in heptad-repeat	K^{22}	PI	Fikkert02										++				0.047	0

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Residue[1]	Comments	Substitution	Isolate[2]	Reference	Expression (cell lysate)[3]	Expression (cell surface)[4]	gp160 processing[5]	gp120 association[6]	CD4-binding[7]	CD4-induced shedding[8]	Cell-cell fusion[9]	Virion incorporation[10]	Virus entry[11]	Viral Replication[12]	Oligomerization (gp160/gp140)[13]	Trimerization (SOS gp140)[14]	Thermal stability (gp41 core)[15]	B-clade entropy	C-clade entropy
L555	d in heptad-repeat	G	HXB2	Cao93	++		–	–			–							0	0
		A	BH8	Poumbourios97	++		–		++		–				++				
		V[21]	JR-FL	Sanders02		–													
		W[21]	JR-FL			–													
		Y[21]	JR-FL			–													
		S[21]	JR-FL			–													
		P[21]	JR-FL			–													
L556	e in heptad-repeat	P	HXB2	Chen94	++		+	–					–					0.047	0
		R	HXB2	Weng98	–						–		–						
		E	HXB2		–						–		–						
		A	HXB2		+	–							–						
		D	HXB2	Weng00	++		++					++	–						
		G	HXB2		++		++					++	–						
		K	HXB2		–								–						
		N	HXB2		++		++					++	–						
		A	HXB2	Lu01, Follis02		++	+	++			–		+				++		
		P[21]	JR-FL	Sanders02		++										+			
R557	f in heptad-repeat	P[21]	JR-FL	Sanders02		++										+		0.237	0.334
		M	PI	Wei02										++					
A558	g in heptad-repeat	R	HXB2	Weng98	–								–					0	0
		E	HXB2		+								–						
		C	HXB2	Weng00	++		++					++	–						
		G	HXB2		++		++					++	–						
		T	HXB2		++		++					++	+						
		P[21]	JR-FL	Sanders02		++										+			

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Residue[1]	Comments	Substitution	Isolate[2]	Reference	Expression (cell lysate)[3]	Expression (cell surface)[4]	gp160 processing[5]	gp120 association[6]	CD4-binding[7]	CD4-induced shedding[8]	Cell-cell fusion[9]	Virion incorporation[10]	Virus entry[11]	Viral Replication[12]	Oligomerization (gp160/gp140)[13]	Trimerization (SOS gp140)[14]	Thermal stability (gp41 core)[15]	B-clade entropy	C-clade entropy
I559	a in heptad-repeat	P	HXB2	Chen93, Chen94	++	++	–	–	++		–		–		++			0.047	0
		A	BH8	Poumbourios97	++		–		++		–				++				
		V[21]	JR-FL	Sanders02		+										+			
		F[21]	JR-FL			–										+++			
		N[21]	JR-FL			–										+++			
		P[21]	JR-FL			++	++									+++	–		
		G[21]	JR-FL			+	++									+++	+		
		R[21]	JR-FL			+										+++			
		P	LAI/ JR-FL	Sanders03b										–			–		
		G	LAI/ JR-FL											–			+		
		L	LAI/ JR-FL											++			++		
E560	b in heptad-repeat	P[21]	JR-FL	Sanders02		+++										+		0.217	0
		G[19]	ELI1	Kozak97							+								
A561	c in heptad-repeat	P[21]	JR-FL	Sanders02		+++										+		0.094	0.101
S561		A[28]	MN	Park00										++					
Q562	d in heptad-repeat	L	HXB2	Cao93	++		+	–			–							0	0.101
		A	BH8	Poumbourios97	++		++	+	++		–				++				
		P[21]	JR-FL	Sanders02		+++										+			
Q563	e in heptad-repeat	A	HXB2	Weng00	++		++					++	++					0.047	0
		E	HXB2		++		++					++	–						
		M	HXB2		++		++					++	–						
		G	HXB2		++		++					++	++						
		R	HXB2		++		++					++	+						
		A	HXB2	Lu01, Follis02		++	++	++			++		++				++		
		P[21]	JR-FL	Sanders02		+++										+			
R564	f in heptad-repeat	P[21]	JR-FL	Sanders02		+++										+		0.047	0
H564		N[28]	MN	Park00										++					
		C[26]	HXB2	Rabenstein95											++				
L565	g in heptad-repeat	P	HXB2	Chen94	++	++	+	++	++		–							0.402	0.584
		A	HXB2	Lu01, Follis02		++	++	++			–		–				+		
		P[21]	JR-FL	Sanders02		++										+			

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Residue[1]	Comments	Substitution	Isolate[2]	Reference	Expression (cell lysate)[3]	Expression (cell surface)[4]	gp160 processing[5]	gp120 association[6]	CD4-binding[7]	CD4-induced shedding[8]	Cell-cell fusion[9]	Virion incorporation[10]	Virus entry[11]	Viral Replication[12]	Oligomerization (gp160/gp140)[13]	Trimerization (SOS gp140)[14]	Thermal stability (gp41 core)[15]	B-clade entropy	C-clade entropy
L566	a in heptad-repeat	G	HXB2	Cao93		++	+	+		–	–		+					0.047	0
		P	HXB2	Chen93, Chen94	++	++	+	+	++		–		–		++				
		A	BH8	Poumbourios97	++		–		++		–				++				
		V[23]	BH8	Earl93		++	++		++						++				
		V[21]	JR-FL	Sanders02		+	++									++	++		
		I[21]	JR-FL			–										+			
		N[21]	JR-FL			+										++			
		T[21]	JR-FL			+										++			
		P[21]	JR-FL			+	++									+			
		K[21]	JR-FL			–										+			
Q567	b in heptad-repeat	R	LAI	Sanders03a										++			++	0.177	0
L568	c in heptad-repeat	A	HXB2	Cao93	++	++	+	++	++	++	–		+					0	0
		P	HXB2	Chen94	++	++	+	+	++		–								
		A	HXB2	Ji00													+		
T569	d in heptad-repeat	A	BH8	Poumbourios97	++		–		++		–				++			0	0.101
		C	HXB2	Farzan98			–												
		S[21]	JR-FL	Sanders02		+										+			
		P[21]	JR-FL			+	++									++	+		
		K[21]	JR-FL			+										++			
		E[21]	JR-FL			–													
V570	e in heptad-repeat	R	HXB2	Weng98	++	++			++		–	++	–					0	0
		E[35]	HXB2		++	++			++			++							
		A	HXB2	Weng00	++		++					++	–						
		D	HXB2		++		++					++	–						
		E	HXB2		++		++					++	–						
		G	HXB2		++		++					++	–						
		I	HXB2		++		++					++	++						
		A	HXB2	Lu01, Follis02		++	++	++			–		–				+		
W571	f in heptad-repeat	R	HXB2	Cao93	++	++	+	++	++	–	–		–					0	0
		R	HXB2	Ji00													++		
		C[26]	HXB2	Rabenstein95											++				
G572	g in heptad-repeat	G	HXB2	Weng98	++	–			++		–	–	–					0	0
		A	HXB2	Lu01		++	++	++			–						+++		

gp41 ectodomain

Residue[1]	Comments	Substitution	Isolate[2]	Reference	Expression (cell lysate)[3]	Expression (cell surface)[4]	gp160 processing[5]	gp120 association[6]	CD4-binding[7]	CD4-induced shedding[8]	Cell-cell fusion[9]	Virion incorporation[10]	Virus entry[11]	Viral Replication[12]	Oligomerization (gp160/gp140)[13]	Trimerization (SOS gp140)[14]	Thermal stability (gp41 core)[15]	B-clade entropy	C-clade entropy
I573	a in heptad-repeat	L	HXB2	Dubay92	++		++	++			++	++		++	++			0.083	0
		V	HXB2		++	++	++	++			++	++		++	++				
		A	HXB2		++		++	++			+	++		+	++				
		G	HXB2		++	++	++	++			–	++		–	++				
		E	HXB2		++	++	++	++			–	++		–	++				
		D	HXB2		++		++	++			–	++		–	++				
		S	HXB2		++		++	++			–	++		–	++				
		P^{24}	HXB2	Bernstein95											–				
		A^{24}	HXB2												+				
		D^{24}	HXB2												–				
		A^{25}	HXB3	Shugars96											++				
		S^{25}	HXB3												–				
		P	HXB2	Chen93, Chen94	++	+++	+	+	++		–		–		++				
		P^{26}	HXB2, LAI	Wild94	++		++	+			–						–		
		A^{26}	HXB2, LAI		++	++	++	++			+			+			–		
		S^{26}	HXB2, LAI		++	++	++	++			–			–			–		
		P^{26}	HXB2	Rabenstein95											–				
		D^{26}	HXB2												–				
		S^{26}	HXB2												–				
		S	168P	Liu01													–		
		T	168P			++	++	++			++	++	++				+		
		V	LAI	Sanders03a										++			++		
		A	BH8	Poumbourios97	++		++	++	++		–				++				
		V	HXB2	Markosyan02													++		
		A	HXB2														+		
		S	HXB2														+		
		P	HXB2														–		
		L^{21}	JR-FL	Sanders02		++										+			
		F^{21}	JR-FL			++										+			
		Y^{21}	JR-FL			++										+			
		Q^{21}	JR-FL			++										+			

gp41 ectodomain

Residue[1]	Comments	Substitution	Isolate[2]	Reference	Expression (cell lysate)[3]	Expression (cell surface)[4]	gp160 processing[5]	gp120 association[6]	CD4-binding[7]	CD4-induced shedding[8]	Cell-cell fusion[9]	Virion incorporation[10]	Virus entry[11]	Viral Replication[12]	Oligomerization (gp160/gp140)[13]	Trimerization (SOS gp140)[14]	Thermal stability (gp41 core)[15]	B-clade entropy	C-clade entropy
I573		N^{21}	JR-FL			++										+			
(cont)		T^{21}	JR-FL			++										+			
		P^{21}	JR-FL			++										+			
		G^{21}	JR-FL			++										+			
		K^{21}	JR-FL			++										+			
K574	b in heptad-repeat	R	BH8	McInerney98	++		++	++	++	++	+							0	0
L576	d in heptad-repeat	P	HXB2	Chen94	++		+	+	++		–							0	0
		A	BH8	Poumbourios97	++		–		++		–				++				
		C^{27}	HXB2	Farzan98	++	+	–								+++				
		V^{21}	JR-FL	Sanders02		–										+			
		F^{21}	JR-FL			–										+			
		Y^{21}	JR-FL			–										+			
		Q^{21}	JR-FL			–										+			
		N^{21}	JR-FL			–										+			
		G^{21}	JR-FL			–										+			
		K^{21}	JR-FL			–										+			
Q577	e in heptad-repeat	R	HXB2	Weng98	++	++			++			++	–					0.047	0.173
		E	HXB2		++	++			++		+	+	+						
		A	HXB2	Weng00	++		++					++	+						
		D	HXB2		++		++					++	++						
		E	HXB2		++		++					++	+						
		G	HXB2		++		++					++	++						
		M	HXB2		++		++					++	+						
		C^{27}	HXB2	Farzan98	++	+	–								+++				
		A	HXB2	Lu01		++	++	++			++						++		
A578	f in heptad-repeat	G^{27}	HXB2	Farzan98	++	+	–								+++			0.047	0.483
R579	g in heptad-repeat	G	HXB2	Weng00	++		+					++	–					0	0.101
		A	HXB2	Lu01		++	+	++			–						++		

gp41 ectodomain

Residue[1]	Comments	Substitution	Isolate[2]	Reference	Expression (cell lysate)[3]	Expression (cell surface)[4]	gp160 processing[5]	gp120 association[6]	CD4-binding[7]	CD4-induced shedding[8]	Cell-cell fusion[9]	Virion incorporation[10]	Virus entry[11]	Viral Replication[12]	Oligomerization (gp160/gp140)[13]	Trimerization (SOS gp140)[14]	Thermal stability (gp41 core)[15]	B-clade entropy	C-clade entropy
I580	a in heptad-repeat	P	HXB2	Chen94	++	++	+	–	++		–							0.432	0.173
		A	BH8	Poumbourios97	++		++	++	++		–				++				
		L[21]	JR-FL	Sanders02		++										+			
		H[21]	JR-FL			++										+			
		T[21]	JR-FL			++										+			
		P[21]	JR-FL			++										+			
		G[21]	JR-FL			++										+			
L581	b in heptad-repeat	Q[28]	MN	Park00										++				0	0
A582	c in heptad-repeat	T[28]	PI	Reitz88										++				0.094	0.101
		C[26]	HXB2	Rabenstein95											++				
V583	d in heptad-repeat	A	BH8	Poumbourios97	++		+	++	++		–				++			0.244	0.503
		C	HXB2	Farzan98			–												
		L[21]	JR-FL	Sanders02		++										+			
		Q[21]	JR-FL			++										+			
		N[21]	JR-FL			++										+			
		S[21]	JR-FL			++										+			
		P[21]	JR-FL			++										+			
		R[21]	JR-FL			++										+			
		K[21]	JR-FL			++										+			
E584	e in heptad-repeat	A	HXB2	Cao93		++	–	–		+	–		–					0	0
		Q	BH8	Maerz01	++	++	++	+			+								
		D	BH8		++		++				+								
		N	BH8		++		++				–								
Y586	f in heptad repeat	R	HXB2	Weng98	++	+			++			+	–					0	0.101
		E	HXB2		++	+			++			+	–						
		C[29]	HXB2	Farzan98			–												
L587	a in heptad-repeat	P	HXB2	Chen93, Chen94	++	++	++	–	++		–		–		++			0	0
		A	BH8	Poumbourios97	++		++	++	++		–				++				
		C[29]	HXB2	Farzan98			–												
		A[21]	JR-FL	Sanders02		–										+			
		P[21]	JR-FL			–										+			
		R[21]	JR-FL			–										+			
		D[21]	JR-FL			–										+			
		E[21]	JR-FL			–										+			

gp41 ectodomain

Residue[1]	Comments	Substitution	Isolate[2]	Reference	Expression (cell lysate)[3]	Expression (cell surface)[4]	gp160 processing[5]	gp120 association[6]	CD4-binding[7]	CD4-induced shedding[8]	Cell-cell fusion[9]	Virion incorporation[10]	Virus entry[11]	Viral Replication[12]	Oligomerization (gp160/gp140)[13]	Trimerization (SOS gp140)[14]	Thermal stability (gp41 core)[15]	B-clade entropy	C-clade entropy
K588		R	BH8	McInerney98	++		++	++	++	++	++							1.112	0.775
D589		L	HXB2	Cao93	++	++	+++	+	++	+	–		+					0	0.101
		C[30]	JR-FL	Binley00		++													
		K	BH8	Maerz01	++	++	++	+			–								
Q591		A	BH8	Maerz01	++	++	++	++			++							0.083	0.101
		K	BH8		++		++				++								
		L	LAI	Sanders03c										+					
L592		V	BH8	Maerz01	++		++				++							0	0.101
		A	BH8		++		++				++								
L593		V	BH8	Maerz01	++		++				+		–					0.143	0
		A	BH8		++	++	++	–			+		–						
		Q	LAI	Sanders03c										+/–					
I595		F[31]	PI	Moore93										++				0.162	0.555
W596		M	HXB2	Cao93, Cao94	++	++	++	+	++		–		++	++	++			0	0
		Y	LAI, NL4-3	Rovinski99			++					++							
		A	LAI, NL4-3				–					+							
		C[30]	JR-FL	Binley00		++													
		F	BH8	Maerz01	++	++	++	+			++		++						
		H	BH8		++		++				+								
		L	BH8		++	++	++	+			+								
G597		P	BH8	Maerz01	++	++	++	–			–							0	0
		A	BH8		++	++	++	–			–								
		S	BH8		++	++	++	–			–								
C598		S	HXB2	Dedera92a	++		–				–							0	0
		S[23]	BH8	Earl93		++	++		++						++				
		G	HXB2	Syu91	++		–							–					
		A	LAI	Van Anken03										–					
G600		A	LAI, NL4-3	Rovinski99			++					++						0	0.101

gp41 ectodomain

Residue[1]	Comments	Substitution	Isolate[2]	Reference	Expression (cell lysate)[3]	Expression (cell surface)[4]	gp160 processing[5]	gp120 association[6]	CD4-binding[7]	CD4-induced shedding[8]	Cell-cell fusion[9]	Virion incorporation[10]	Virus entry[11]	Viral Replication[12]	Oligomerization (gp160/gp140)[13]	Trimerization (SOS gp140)[14]	Thermal stability (gp41 core)[15]	B-clade entropy	C-clade entropy
K601		R	BH8	McInerney98	++		++	++	++	++	++							0.218	0
		R	LAI, NL4-3	Rovinski99			++					++							
		E	LAI, NL4-3				++					++							
		E	BH8	Merat99	++		+				++								
		E	BH8	Maerz01	++	++	++	+			++								
		H	BH8		++		++	+			++								
		Q	BH8		++		++	+			++								
		A	BH8		++		++				++								
C604		S	HXB2	Dedera92a	++		–				–							0.047	0
		S[23]	BH8	Earl93		++	++		++						++				
		G	HXB2	Syu91	++		–							–					
		A	LAI	Van Anken03										–					
T605		C[30]	JR-FL, HXB2, DH123, 89.6, GUN1-wt	Binley00		++	++	+++	++						+			0.177	0.173
		C	LAI	Sanders03c										++					
		Y	LAI											++					
V608		S	HXB2	Cao93			–	–			–							0.094	0.101
		C[30]	JR-FL	Binley00		++													
P609		C[30]	JR-FL	Binley00		++												0.047	0.101
W610		C[30]	JR-FL	Binley00		++												0.047	0
		F	BH8	Maerz01	++	++	++	–			–								
		H	BH8		++	++	++	–			–								
N611	Glycosylation site	Q	HXB2	Dedera92b	++		++	++			+			++	++			0.141	0
		H	HXB2	Lee92	++		++					++		+					
		S	NL4-3	Dash94	++	++	++				++								
		Q	SHIV-KB9	Johnson01	++		++							++					
S613	Glycosylation site N611	A	HXB2	Lee92	++		++							+				0.94	0.274

gp41 ectodomain

Residue[1]	Comments	Substitution	Isolate[2]	Reference	Expression (cell lysate)[3]	Expression (cell surface)[4]	gp160 processing[5]	gp120 association[6]	CD4-binding[7]	CD4-induced shedding[8]	Cell-cell fusion[9]	Virion incorporation[10]	Virus entry[11]	Viral Replication[12]	Oligomerization (gp160/gp140)[13]	Trimerization (SOS gp140)[14]	Thermal stability (gp41 core)[15]	B-clade entropy	C-clade entropy
N616	Glycosylation site	Q	HXB2	Dedera92b							+			++				0.237	0
		Q[23]	BH8	Earl93		++	++		++						++				
		H	HXB2	Lee92	++		++					++		++					
		S	NL4-3	Dash94	++	++	++				++								
		Q	BH10	Perrin98	++		++				+								
		Q	SHIV-KB9	Johnson01	++		++							++					
K617		R	BH8	McInerney98	++		++	++	++	++	++							0.348	0.658
S618	Glycosylation site N616	A	HXB2	Lee92	++		++	–						–				0.495	0.483
N624	d in heptad-repeat	H	HXB2	Lee92	++		++					++		+				1.153	1.305
	Glycosylation site (N625 in most isolates)	Q	BH10	Perrin98	++		++				++								
		Q	SHIV-KB9	Johnson01	++		++							++					
N625	e in heptad-repeat	Q[23]	BH8	Earl93		++	++		++						++			0.047	0.274
	Glycosylation site																		
T626	f in heptad-repeat	M	HXB2	Cao93	++	–	–	–		–	–		–					0.244	0.444
	Glycosylation site N624																		
		M[28]	SHIV-HXBc2P	Si01										++					
W628	a in heptad-repeat	M	HXB2	Cao93			–	–		–	–							0	0
		A	HXB2	Weng00	++		–					++	–						
		F	HXB2		++		–					++	–						
		A	HXB2	Wang02		++	–	++			–						+		
W631	d in heptad-repeat	A	HXB2	Wang02		++	–	++			–						–	0	0.101
D632	e in heptad-repeat	N[32]	BH10	Perrin98	++		++				–							0.591	0.287
R633	f in heptad-repeat	G	PI	Wei02										++				0.55	0.451
I635	a in heptad-repeat	A	HXB2	Wang02		++	–	++			–						+	0.047	0.173

gp41 ectodomain

Residue[1]	Comments	Substitution	Isolate[2]	Reference	Expression (cell lysate)[3]	Expression (cell surface)[4]	gp160 processing[5]	gp120 association[6]	CD4-binding[7]	CD4-induced shedding[8]	Cell-cell fusion[9]	Virion incorporation[10]	Virus entry[11]	Viral Replication[12]	Oligomerization (gp160/gp140)[13]	Trimerization (SOS gp140)[14]	Thermal stability (gp41 core)[15]	B-clade entropy	C-clade entropy
N637	c in heptad-repeat	K[22]	PI	Baldwin03										++				0.141	0.101
	Glycosylation site	Q	HXB2	Dedera92b							++			++					
		Q[23]	BH8	Earl93		++	++		++						++				
		H	HXB2	Lee92	++		++					++		–					
		S	NL4-3	Dash94	++	–	–				–								
		Q	BH10	Perrin98	++		++				++								
		Q	SHIV-KB9	Johnson01	++		++							++					
Y638	d in heptad-repeat	A	HXB2	Wang02		++	++	++					++				++	0.13	0
T639	e in heptad-repeat	V	HXB2	Lee92	++		++							+				0.083	0.202
	Glycosylation site N637	A	HXB2	Cao93	++	–	–			–	–								
I642	a in heptad-repeat	A	HXB2	Wang02		++	–	++			–						++	0.094	0
		A	HXB2	Markosyan02													++		
		S	HXB2														++		
H643	b in heptad-repeat	Y[20]	LAI	Bahbouhi01	++		++					++		++				0.115	0
		Y	LAI	Sanders03a										++					
L645	d in heptad-repeat	A	H64333	Wang02		++	++	++					++				++	0	0
E647	f in heptad-repeat	L	HXB2	Cao93		++	+++	+			++		++					0.188	0.173
S649	a in heptad-repeat	A	HXB2	Wang02		++	++	++					++				++	0.401	0
Q652	d in heptad-repeat	L	HXB2	Cao93		++	++	+			++		++					0.047	0.101
		L	HXB2	Shu00													++		
		A	HXB2	Wang02		++	++	++					++				++		
K655	g in heptad-repeat	R[33]	BH8	Poumbourios95	++		++	++			++							0.213	1.093
N656	a in heptad-repeat	L	HXB2	Cao93	++	++	+	++	++	++	–		+					0	0
L663	2F5 epitope	F	HXB2	Cao93		++	+++	++			++		++					0.047	0.101
K665	2F5 epitope	R[33]	BH8	Poumbourios95	++		++	++			++							0.451	0.922
W666	2F5 epitope	P	HXB2	Cao93		++	++	++			++		++					0.047	0.101
		A	HXB2, NL4-3	Salzwedel99	++		++	++			++								
S668	2F5 epitope	N[28]	HXB2	Back93										++				0.497	0.573
L669		P	HXB2	Cao93		+++	++	+		+++	++		++					0.047	0
W670		A	HXB2, NL4-3	Salzwedel99	++		++	++			++							0.047	0
N671	4E10/z13 epitope	P	HXB2	Cao93		++	++	++			++		++					0.713	0.945

gp41 ectodomain

Residue[1]	Comments	Substitution	Isolate[2]	Reference	Expression (cell lysate)[3]	Expression (cell surface)[4]	gp160 processing[5]	gp120 association[6]	CD4-binding[7]	CD4-induced shedding[8]	Cell-cell fusion[9]	Virion incorporation[10]	Virus entry[11]	Viral Replication[12]	Oligomerization (gp160/gp140)[13]	Trimerization (SOS gp140)[14]	Thermal stability (gp41 core)[15]	B-clade entropy	C-clade entropy
W672	4E10/z13 epitope	S	HXB2	Cao93	++	++	++	+		+++	++		++					0	0
		S	HXB2, NL4-3	Salzwedel99	++		++	++			++								
		P	HXB2, NL4-3		++		++	++			++	–	+						
		F	HXB2, NL4-3		++		++	++			++	+	+						
F673	4E10/z13 epitope	P	HXB2	Cao93	++	++	++	+			++		++					0.94	0
		S[34]	HXB2	Stern95							++			++					
N674	4E10/z13 epitope	H	HXB2	Lee92	++		++					++		++				1.038	1.375
		S	NL4-3	Dash94	++	++	++				++								
		D[28]	SHIV-HXBc2P	Si01										++					
I675	4E10/z13 epitope	S	HXB2	Cao93		++	++	+			++		++					0	0
		M[28]	HXB2	Back93										++					
N677		R	HXB2	Cao93		++	++	+			++		++					1.237	0.769
W678		A	HXB2	Cao93		++	++	+			++		++					0	0
		A	HXB2, NL4-3	Salzwedel99	++		++	++			++								
W680		A	HXB2, NL4-3	Salzwedel99	++		++	++			++							0.047	0.101
Y681		P	HXB2	Cao93			++	++			++		++					0	0
K683		R	BH8	McInerney98	++		++	++	++	++	++							0.375	0.325

Table footnotes:

[1] Residue numbering is based on HXB2 gp160, although the amino-acids studied may be different in the isolate used. The one-letter code for amino acids is used

[2]PI: primary isolate

[3]As assessed by western blot or immunoprecipitation. –, minimal or no expression; +, reduced expression; ++, expression similar to WT; +++, increased expression

[4]As assessed by surface biotinylation, iodination or FACS. When soluble gp140 constructs were used, the relative secretion levels (western blot or immunoprecipitation) are given. –, minimal or no expression; +, reduced expression; ++, expression similar to WT; +++, increased expression

[5]As assessed by western blot or immunoprecipitation in combination with densitometric measurements. –, minimal or no processing; +, reduced processing; ++, processing similar to WT; +++, increased processing

[6]As assessed by western blot or immunoprecipitation in combination with densitometric measurements. –, minimal or no association; +, reduced association; ++, association similar to WT; +++, increased association

[7]As assessed by immunoprecipitation with CD4-based reagents. ++, similar to WT; +++, increased CD4 binding

[8]As assessed by immunoprecipitation. –, no shedding; +, reduced shedding; ++, shedding similar to WT; +++, increased shedding. Note that CD4-induced shedding and to a lesser extent gp120 association (*i.e.*, the reverse of shedding), when measured in laboratory isolates, might be diminished in primary isolates that can retain gp120 more efficiently.

[9]As assessed by syncytium formation or reporter gene assays. –, fusion lower than 3% of WT; +, fusion between 3 and 30% of WT; ++, fusion greater than 30% of WT

[10]As assessed by western blot or immunoprecipitation. –, minimal or no incorporation; +, reduced incorporation; ++, incorporation similar to WT

[11]As assessed by various assays (replication complementation, use of reporter genes, p24 production). –, entry lower than 3% of WT; +, entry between 3 and 30% of WT; ++, entry greater that 30% of WT

[12]–, no apparent replication; +, replication with a delay of more than 2 days compared to WT; ++ replication similar to WT

[13]As assessed by sucrose gradient fractionation, immunoprecipitation, velocity sedimentation or FPLC, unless indicated otherwise. –, oligomerization below 25% of WT; +, oligomerization between 25% and 50% of WT; ++, oligomerization similar to WT. No distinction between dimerization, trimerization or tetramerization is made.

[14]As assessed by Blue Native-PAGE. +, trimerization similar to WT SOS gp140 (occasional trimerization); ++, slightly more trimerization than in WT; +++, significantly more trimerization than in WT.

[15]As analyzed using the N34(L6)C28 or N36(L6)C34 peptide model, unless indicated otherwise. –, melting temperature (T_m) below 40°C; +, T_m between 40°C and 60°C; ++, T_m between 60°C and 80°C; +++, T_m over 80°C

[16]Analyzed in a double mutant, A512V + F519L

[17]Four amino-acid insertion GIPA

[18]Six amino-acid insertion IHRWIA

[19]Involved in cell line adaptation

[20]Identified in an isolate which is resistant to the furin inhibitor (α1-PDX)

[21]Analyzed in soluble SOS gp140 constructs and so also contain the A501C and T605C substitutions

[22]Involved in T-20 resistance

[23]Analyzed in soluble gp140

[24]Analyzed in an N-peptide/Protein A fusion protein

[25]Analyzed in an N-peptide/maltose binding protein (MBP) fusion protein

[26]Thermal stability (74) or oligomerization (53) of N-peptides analyzed in the absence of C-peptides

[27]Analyzed in a triple mutant L576C + Q577C + A578G

[28]Involved in neutralization resistance

[29]Analyzed in a double mutant Y586C + L587C

[30]Analyzed in combination with gp120 cysteine substitutions in the context of soluble gp140

[31]Involved in resistance to soluble CD4

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[32]Generates a new glycosylation site
[33]Analyzed in a double mutant K655R + K665R
[34]Analyzed in a double mutant A582T + F673S
[35]Data on this mutant were corrected in reference 73

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Web-based Tools for Vaccine Design

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Introduction

Computational methods used in vaccine design have been changing drastically in recent years. In classical immunological research results could be recorded by pen and pencil or in a spreadsheet, but new experimental high-throughput methods such as sequencing, DNA arrays, and proteomics have generated a wealth of data that are not efficiently handled and mined by these approaches. This has fueled the rapid growth of the field of Immunological Bioinformatics (or Immunoinformatics) that addresses how to handle these large amounts of data in the field of immunology and vaccine design. Many of the methods have been made available on the Internet and can be used by experimental researchers without expert knowledge of bioinformatics. This review attempts to give an overview over the methods currently available and to point out the strengths and weaknesses of the different methods.

Immunological processes described by prediction servers

Only a small fraction of the possible peptides that can be generated from proteins of pathogenic organisms actually generate an immune response. In order to be presented to CD8+ T cells a precursor peptide must be generated by the proteasome. This peptide may be trimmed at the N-terminal by other peptidases in the cytosol (Levy et al., 2002). It must then bind to the transporter associated with antigen processing (TAP) in order to be translocated to the endoplasmatic reticulum (ER). Here it can be trimmed N-terminally by the aminopeptidase associated with antigen processing (ERAAP) while it binds to the major histocompatibility complex class I (MHC I) molecule (Serwold, 2002). Hereafter it is transported to the cell surface. Only half the peptides presented on the cell surface are immunogenic probably due to the limited size of the T cell receptor (TCR) repertoire. The most selective step is binding to the MHC I molecule, since only 1/200 binds with an affinity strong enough to generate an immune response (Yewdell, 1999). For comparison the selectivity of TAP binding is reported to be 1/7 (Uebel *et al*., 1997). This all happens in competition with other peptides so in order for a peptide to be immunogenic (immunodominant) it must go through the above described process more efficiently than other peptides produced in a given cell (Reviewed by Yewdell, 1999).

Whereas the MHC I molecule mainly samples peptides from the cytosol, the MHC II molecule presents peptides from endocytosed proteins. Unfolded polypeptides bind to MHC II in the endocytic organelles (Reviewed by Castllino, 1997). Both MHC I and MHC II are highly polymorphic, and the specificity of the alleles are often very different. Different individuals will thus typically react to a different set of peptides from a pathogen.

The specificity of some of the processes involved in antigen presentation can be predicted from the amino acid sequence. This can for example be used to select epitopes for use in a vaccine, and help to understand the role of the immune system in infectious diseases, autoimmune diseases and cancers. Below we describe a number of resources available on the web that can perform such predictions.

Databases of MHC binding peptides

Several databases of MHC binding peptides now exist on the web (Table 1).

SYFPEITHI: The SYFPEITHI database contains information on peptide sequences, anchor positions, MHC specificity, source proteins, source organisms, and publication references. The database comprise approximately 3500 peptide sequences known to bind class I and class II MHC molecules and is based on previous publications on T-cell epitopes and MHC ligands from many species (Rammensee, 1999).

MHCPEP: The other major database of MHC binding peptides, MHCPEP, (Brusic, 1997) comprises over 13,000 peptide sequences known to bind MHC

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molecules. Entries were compiled from published reports as well as from direct submissions of experimental data. Each entry contains the peptide sequence, its MHC specificity and, when available, experimental method, observed activity, binding affinity, source protein, anchor positions, and publication references. Unfortunately the database has since June 1998 been static. The database can be downloaded as an ASCII file.

JenPep: The JenPep database is a newer database that contains quantitative binding data of peptides to MHC and TAP, as well as T cell epitopes (Blythe, 2001). The database contains more than 8000 entries .

FIMM: The database by Schoenbach & Brusic is a functional database of molecular immunology. The database contains 571 antigens and 1591 peptides (Schonbach et al., 2002)

MHCBN: (Bhasin, 2002) is a database of MHC binding and non-binding peptides containing 14,816 binders, 1,782 non-binders and 5,456 T-cell epitope entries.

HLA Ligand/Motif database: This site's database can be searched by defining allele and specificity, amino acid pattern, ligand/motif in sequence of amino acids, author's last name, or advanced search with more criteria.

HIV Molecular Immunology database: The HIV Molecular Immunology Database is an annotated, searchable collection of HIV-1 cytotoxic and helper T-cell epitopes and antibody binding sites. The goal of the database is to provide a comprehensive listing of defined HIV epitopes (Korber *et al*., 2001).

EPIMHC: MHC ligand database that can be searched based on sequence, length, class, species, and on whether a ligand is an epitope or not.

NIH will over the next five to seven years fund an "Immune Epitope Database and Analysis Program"[1] to design, develop, populate, and maintain a publicly accessible, comprehensive Immune Epitope Database containing linear and conformational antibody epitopes and T cell epitopes. This database may eventually incorporate most of the data from the above described databases.

Prediction of MHC binding

Several peptide-MHC binding prediction servers exist on the web (Table 2). As indicated in the table some of the web based methods also allow prediction of binding to Class II molecules. Most methods available on the web for predicting MHC-peptide binding are matrix methods. Parameters are often derived from pool sequencing of ligands. Matrices or hidden Markov models may however also be derived from a set of ligand sequences. In these methods the amino acid on each position in the motif gives an independent contribution to the prediction score. Neural networks are able to make more accurate predictions if correlations between positions exist, and there are enough data to model them. This has the potential advantage that it can take correlations between different positions in the binding motif into account.

BIMAS: The BIMAS method was developed by Parker *et al*., (1994). The method is based on coefficient tables deduced from the published literature. For HLA-A2, peptide binding data were combined together to generate a table containing 180 coefficients (20 amino acids x 9 positions), each of which represents the contribution of one particular amino acid residue at a specified position within the peptide (Parker *et al*., 1994).

SYFPEITHI: The SYFPEITHI prediction is based on published motifs (pool sequencing, natural ligands) and takes into consideration the amino acids in the anchor and auxiliary anchor positions, as well as other frequent amino acids. The score is calculated according to the following rules: The amino acids of a certain peptide are given a specific value depending on whether they are anchor, auxiliary anchor or preferred residue. Ideal anchors will be given 10 points, unusual anchors 6–8 points, auxiliary anchors 4–6 and preferred residues 1–4 points. Amino acids that are regarded as having a negative effect on the binding ability are given values between -1 and -3 (Rammensee, 1997; 1999). On the SYFPEITHI web site predictions can be made for 5 different MHC II alleles in addition to a number of Class I alleles.

PREDEPP: In this method the peptide structure in the MHC groove is used as a template upon which peptide candidates are threaded, and their compatibility to bind is evaluated by statistical pairwise potentials. This method has the advantage that it does not require experimental testing of peptide binding, and can thus be used for alleles where only limited data are available (Schueler-Furman *et al*., 2000).

Epipredict: Method using synthetic combinatorial peptide libraries to describe peptide-HLA class II interaction in a quantitative way. The binding contribution of every amino acid side chain in a class II-ligand is described by allele-specific two-dimensional databases (Jung *et al*., 2001).

Predict: The Predict method use neural networks to predict Class I, II and TAP binding (Yu *et al*., 2002).

[1] www.niaid.nih.gov/contract/archive/rfp0331.pdf

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Propred: The Propred method (Singh, 2001) is based on the matrices published by Sturniolo (1999), and is an implementation and extension of the TEPITOPE program. (Hammer, 1995; Raddrizzani, 2000)). Besides differences that can be attributed to round off errors we have in our tests not seen any differences between the two implementations.

MHCPred: Prediction of binding to 11 different HLA class I alleles using a three-dimensional quantitative structure-activity relationship method (Doytchinova *et al*., 2002).

NetMHC: Prediction of HLA-A2 binding using neural networks. This method predicts quantitatively the binding affinity, and is different from methods performing classification only (binding versus non-binding according to a threshold). The method has been trained using quantitative binding data generated by the same assay (Buus *et al*., 2003), and some predicted binders have been tested for their ability to induce a CTL response in mice and be recognized by CD8+ T-cells from HLA-A2 HIV-1 positive patients (Corbet *et al*., 2003). Two well-known prediction methods, TEPITOPE and EpiMatrix (Meister 1995; De Groot, 1997) that are not available through the web are listed in Table 3. TEPITOPE is popular since it allows prediction of peptides to many different Class II molecules.

Prediction of proteasomal cleavage sites

The C terminal of MHC class I ligands must most likely be cleaved by the proteasome. The proteasome usually generates precursors of MHC ligands with an extension at the N-termini. These precursors can be trimmed at the N-terminal in the ER. The existence of proteasome cleavage sites within epitopes need not abrogate the immune response for such epitopes. They may, however, reduce the availability, and thereby the immunogenecity of a given peptide (Yewdell, 1999). The proteasome thus plays an important role in selecting which peptides are presented to CD8+ T cells. In vertebrates stimulation with IFN-γ leads to the replacement of three subunits of the constitutive proteasome to form the so-called immunoproteasome which has a different specificity (reviewed by Uebel, 1999). Different methods for predicting proteasomal cleavage sites exist on the web (Table 4).

PAProC: Prediction Algorithm for Proteasomal Cleavages is a prediction tool for cleavages by human and yeast proteasomes, based on experimental cleavage data. (Kuttler, 2000; Nussbaum, 2001). An updated version of the PAProC program based on *in vitro* immunoproteasome cleavage data (Toes, 2001) is also in the making according to the PAProC homepage.

FRAGPREDICT comprises two different algorithms. One that aims at predicting potential proteasomal cleavage, based on a statistical analysis of cleavage-determining amino acid motifs present around the scissile bond (Holzhütter *et al*., 1999, 2000). The second algorithm, which uses the results of the cleavage site analysis as an input, provides predictions of major proteolytic fragments.

NetChop: (Kesmir, 2002) is a method based on neural networks that have been trained on different data sets. C Kesmir suggests to use the C-term 2.0 network which was trained on C-terminal cleavage sites of 1,110 publicly available MHC class I ligands for predicting the boundaries of CTL. The specificity of this network may resemble the specificity of the immunoproteasome.

Margalit's group have also recently made their proteasomal cleavage site propensities (Altuvia and Margalit, 2000) available on the net (`bioinfo.md.huji.ac.il/marg/cleavage/index.html`).

Combined predictions

A number of sites providing combined predictions have been developed recently. The MAPPP server (Table 2) allows the user to make an open reading frame (ORF) search combined with MHC binding and proteasomal cleavage site predictions, and Raghava have a prediction server[2] which implements matrices for 47 MHC Class-I alleles and proteasomal and immunoproteasomal models. The NetMHC server allows combination of HLA-A2 and NetChop predictions.

MHC sequence databases

A number of databases containing sequences of proteins of immunological interest exist on the web (Table 5).

HIG: The HLA Sequence Database currently contains 1,596 allele sequences. To date (October 2002), some 263 HLA-A, 501 HLA-B, 125 HLA-C, 6 HLA-E, 1 HLA-F and 15 HLA-G class I alleles have been named. A total of 3 HLA-DRA, 397 HLA-DRB, 22 HLA-DQA1, 53 HLA-DQB1, 20 HLA-DPA1, 100 HLA-DPB1, 4 HLA-DMA, 6 HLA-DMB, 8 HLA-DOA and 8 HLA-DOB class II sequences have also been assigned. There are also 6 TAP1, 4 TAP2 and 54

[2] `www.imtech.res.in/raghava/propred1/index.html`

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MICA sequences. The HLA Sequence Database also contains the comprehensive nomenclature for factors of the HLA system (listings for HLA class I and class II allele names) which is very helpful since the HLA nomenclature is very complicated and cumbersome.

IMGT: IMGT, the international ImMunoGeneTics project, is a collection of databases specializing in Immunoglobulins, T cell receptors and the Major Histocompatibility Complex (MHC) of all vertebrate species. The IMGT project was established in 1989 by the Université Montpellier II and the CNRS (Montpellier, France) and works in close collaboration with the EBI.

ASHI: The American Society for Histocompatibility and Immunogenetics (ASHI) hosts databases of gene and allele frequencies (www.ashi-hla.org/).

MHCDB: "Registered users only" database of MHC sequences. This is an ACeDB-style database holding the Human Major Histocompatibility Database. It is largely superseded by 6ace which is ACeDB-style database of human chromosome 6 from the Sanger Centre.

Other sites

A number of other databases relevant to immunology and vaccine design are listed in Table 6. Table 7 contains a compilation of lists of links. As stated in Table 7 we will also make an HTML version of this article available on the net.

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Table 1: Databases of MHC binding peptides

Name	Principal Investigator	URL	Description
SYFPEITHI	Rammensee	syfpeithi.bmi-heidelberg.com/scripts/MHCServer.dll/home.htm	Database and prediction server for peptides that bind MHC molecules.
MHCPEP	Brusic, Harrison	wehih.wehi.edu.au/mhcpep	Database of MHC binding peptides
JenPep	Flower	www.jenner.ac.uk/JenPep	Database of MHC and TAP binding peptides
FIMM	Schoenbach & Brusic	sdmc.krdl.org.sg:8080/fimm	Database of functional molecular immunology/binding prediction
MHCBN	Raghava	www.imtech.res.in/raghava/mhcbn	Tools for subunit vaccine design
HLA Ligand/Motif Database	Hildebrand	hlaligand.ouhsc.edu	Ligand database/prediction
HIV Molecular Immunology	Korber	hiv-web.lanl.gov/content/immunology/	HIV CTL epitopes
EPIMHC	Reinherz	mif.dfci.harvard.edu/Tools/db_query_epimhc.html	Peptides that bind to MHC molecules

Table 2: HLA Peptide Binding Predictions

Name	URL	Description
BIMAS	bimas.dcrt.nih.gov/molbio/hla_bind	Prediction of MHC class I binding using matrices
SYFPEITHI	syfpeithi.bmi-heidelberg.com/Scripts/MHCServer.dll/EpPredict.htm	Prediction of Class I and II binding
PREDEPP	bioinfo.md.huji.ac.il/marg/Teppred/mhc-bind	MHC Class I epitope prediction
Epipredict	www.epipredict.de/index.html	Prediction of HLA class II restricted binding
Predict	http://sdmc.krdl.org.sg:8080/predict-demo	Prediction of Class I, II and TAP binding
Propred	www.imtech.res.in/raghava/propred	MHC class II prediction
MHCPred	www.jenner.ac.uk/MHCPred	HLA class I predictions
NetMHC	www.cbs.dtu.dk/services/NetMHC	Prediction of HLA-A2 binding using Neural networks
MAPPP	www.mpiib-berlin.mpg.de/MAPPP/expertquery.html	Combined ORF, MHC binding and proteasomal cleavage Registration needed for expert mode

Table 3: Non web MHC binding predictions

Name	URL	Description
TEPITOPE	www.vaccinome.com	PC Program for Class II predictions can be downloaded
EpiMatrix	epivax.com/epimatrix.html	Commercial epitope prediction

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Table 4: Prediction of proteasomal cleavage sites

Name	URL	Description
Paproc	paproc.de	A matrix based method for prediction of protasomal cleavage
FRAGPREDICT	www.mpiib-berlin.mpg.de/MAPPP/cleavage.html	Proteolytic fragment predicter
NetChop	www.cbs.dtu.dk/services/NetChop	A neural network based method for prediction of proteasomal cleavage

Table 5: MHC sequence databases

Name	URL	Description
HIG	www.anthonynolan.org.uk/HIG	HLA sequence database
IMGT	www.ebi.ac.uk/imgt	Sequences of MHC, TCR and immunoglobulin molecules
ASHI	www.ashi-hla.org	Sequences and Gene and Haplotype frequencies
MHCDB	www.hgmp.mrc.ac.uk/Registered/Option/mhcdb.html	Registered users only database of MHC sequences

Table 6: Other sites

Name	URL	Description
HIV Molecular Immunology database	hiv-web.lanl.gov/content/immunology	HIV immunology
School of Crystallography, Birkbeck College, University of London	www.cryst.bbk.ac.uk/pps97/assignments/projects/coadwell/MHCSTFU1.HTM	Structure and Function of the Major Histocompatibility Complex (MHC) Proteins
MHC-Peptide Interaction Database (MPID)	surya.bic.nus.edu.sg/mpid/	Structural information and characterization of MHC peptide interaction
ELF	hiv-web.lanl.gov/content/hiv-db/ALABAMA/epitope_analyzer.html	Epitope Location Finder
ASHI	www.ashi-hla.org	The American Society for Histocompatibility and Immunogenetics

Table 7: Links to lists of links

Name	URL	Description
Syfpeithi	http://syfpeithi.bmi-heidelberg.com/Scripts/MHCServer.dll/Info.htm	Rammensee's links
FIMM	http://sdmc.krdl.org.sg:8080/fimm	Brusic's links
CBS	www.cbs.dtu.dk/courses/27485.imm/links.html	Our links
HLA-RELATED LINKS	home.att.net/ dorak/hla/linkhla.html	Dorak's links
This article	www.cbs.dtu.dk/researchgroups/immunology/webreview.html	The present article in HTML format

Part II

HIV CTL Epitopes

II-A Summary

Part II includes tables, maps, and associated references of HIV-specific CTL epitopes arranged sequentially according to the location of the proteins in the HIV-1 genome. We attempted to make this section as comprehensive as possible, requiring that the epitope be contained within a defined region of a maximum of 30 amino acids, but not that the optimal boundaries be defined. Studies that were based on the analysis of whole proteins are described at the end of each protein section. The same epitope can have multiple entries, and each entry represents a single publication in this section of the database. For more recent updates and useful searching capabilities, please see our web site: `http://hiv-web.lanl.gov/immunology`. For a concise listing of the best defined CTL epitopes, see the summary by Christian Brander and Philip Goulder on page 3 in Part I of this compendium. CTL protein reactions with no well-defined epitopes are listed at the end of each protein section.

Recent studies utilize multiple functions attributed to T cells to define responses, and the simple distinctions of cytotoxic T-cell and helper T-cells have become blurred as more is learned about the range of responses triggered in CD4 and CD8 positive T-cells responding to antigenic stimulus. When adding the most recent studies, we have tried to place T cell responses in a reasonable manner into our traditional helper T cell and CTL sections, and to specify the assay used to measure the response in each study.

II-A-1 CTL Epitope Tables

Each CTL reference has a six part basic entry:

HXB2 Location: The viral strain HXB2 (GenBank Accession Number K03455) is used as a reference strain throughout this publication. The position of the defined epitope location relative to the sequence of the HXB2 protein is indicated. The numbering in this table corresponds to the protein maps. Because of HIV-1 variation the epitope may not actually be present in HXB2, rather the position in HXB2 indicates the position aligned to the epitope. HXB2 was selected as the reference strain because so many studies use HXB2, and because crystal structures for HXB2-related proteins are often available. The precise positions of an epitope on the HXB2 reference strain can be readily obtained using the interactive position locator at our web site: `http://hiv-web.lanl.gov/content/hiv-db/LOCATE_SEQ/locate.html`.

Author Location: The amino acid positions of the epitope boundaries and the reference sequence are listed as given in the primary publication. Frequently, these positions as published are imprecise, and do not truly correspond to the numbering of the sequence, but they provide a reasonable guide to the peptide's approximate location in the protein. Also, in many cases the reference sequence identification was not provided, and in such cases it is not possible to use these numbers to specify precise locations.

Epitope Sequence: The amino acid sequence of the epitope of interest as defined in the reference, based on the reference strain used in the study defining the epitope. On occasions when only the position numbers and not the actual peptide sequence was specified in the original publication, we tried to fill in the peptide sequence based on the position numbers and reference strain. If the sequences were numbered inaccurately by the primary authors, or if we made a mistake in this process, we may have misrepresented the binding site's amino acid sequence. Because of this uncertainty, epitopes that were not explicitly written in the primary publication, that we determined by looking up the reference strain and the numbered location, are followed by a question mark in the table.

Immunogen: The original stimulus of the CTL response. Often this is an HIV-1 infection. If a vaccine was used as the original antigenic stimulation, not a natural infection, this is noted on a separate line, and additional information about the vaccine antigen is provided as available.

Species(HLA): The species responding and HLA or MHC specificity of the epitope.

Reference: The primary reference (sometimes two or more directly related studies are included). Details for some of the earlier references are in Part V.

Following the entry for a given CTL epitope are brief comments explaining the context in which the epitope was studied and what was learned about the epitope in a given study.

II-A-2 HIV Protein Epitope Maps

All HIV CTL epitopes mapped to within a region of 21 amino acids or less are indicated on the HIV protein epitope maps. The location and HLA restriction elements of CTL epitopes are indicated on protein sequences of HXB2. These maps are meant to provide the relative location of defined epitopes on a given protein, but the HXB2 sequence may not actually carry the epitope of interest, as it may vary relative to the sequence for which the epitope was defined. Epitopes with identical boundaries and HLA fields are included in the maps only once. If one laboratory determines HLA presenting molecules at the serotype level (example: A2) and another at the genotype level (example: A*0201) both will be included in the map. MHC specificities are indicative of the host species; when no MHC presenting molecule is defined, the host species is noted.

II-A-3 Alignments

To conserve space, no epitope alignments are provided in this book, but they can be generated using the CTL epitope search tool at `http://hiv-web.lanl.gov/immunology`. All epitopes are aligned to the HXB2 sequence, with the sequence used to define the epitope indicated directly above it. Sequences are sorted by their subtype and country of origin.

The master alignment files from which the epitope alignments were created are available at our web site (`http://hiv-web.lanl.gov/ALIGN_CURRENT/ALIGN-INDEX.html`). The alignments were modified in some cases to optimize the alignment relative to the defined epitope and minimize insertions and deletions; epitope alignments are generated by anchoring on the C-terminal residue. A dash indicates identity to the consensus sequence, and a period indicates an insertion made to maintain the alignment. Stop codons are indicated with a `$`, and frameshifts by a `#`, or ambiguous codons (nucleotide was `r`, `y`, or `n`) by an `x`; they are inserted to maintain the alignments. In consensus sequences an upper case letter indicates the amino acid was present in all sequences, a lower case letter indicates the amino acid was present in most sequences in a given position, and a question mark indicates two or more amino acids were represented with equal frequency.

II-B HIV CTL Epitope Tables

All HIV CTL epitopes arranged by protein position. The table entries are sorted in a nested way—first by protein, then by HXB2 start location and finally by HLA. CTL reactions against proteins with undefined epitopes are listed at the end of the protein which stimulated the response.

II-B-1 p17 CTL Epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17 (11–19)		GELDRWEKI	HIV-1 infection	human (B*4002)	Sabbaj2002b
	• Epitope name: Gag-GI9 • This study monitored epitope responses in HIV-1 infected minority women living in the United States • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release • This epitope was newly defined in this study • Patient 01RCH46 was Hispanic, on HAART, and had a viral load of 21000 and CD4 count of 623 – she also recognized KETINEEAA p24(70-78), HLA B*4002, and TAFTIPSI, RT(128-135), HLA A*0217 • Among HIV+ individuals who carried HLA B40, 2/5 (40%) recognized this epitope				
p17 (18–26)	p17 (18–26 IIIB)	KIRLRPGGK		human (A*0301)	Brander2001
	• C. Brander notes that this is an A*0301 epitope				
p17 (18–26)	p17 (18–26 SF2)	KIRLRPGGK	HIV-1 infection	human (A*0301)	Altfeld2001a
	• HIV+ individual AC-06 was tested for reactive overlapping peptides spanning all HIV-1 proteins in an ELISPOT and was found to react with 12 peptides from 7 proteins, suggesting that the breadth of CTL responses are underestimated if accessory proteins are not included in the study • The reactive peptide p17 gag WEKIRLRPGGKKKYK contained two A*0301-restricted epitopes, KIRLRPGGK and RLRPGGKKK A*0301				
p17 (18–26)	p17 (18–26 IIIB)	KIRLRPGGK	HIV-1 infection	human (A3)	Wilson1996
	• Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study • KIRLRPGGR and RIRLRPGGR, naturally occurring variants, were found in mother, and are escape mutants				
p17 (18–26)	p17 (18–26)	KIRLRPGGK	in vitro stimulation	human (A3)	Zarling1999
	• This study compares the ability of macrophages and dendritic cells to stimulate primary responses in CD8+ lymphocytes isolated from HLA-appropriate HIV-uninfected donors using peptide-pulsed APC – the dendritic cells performed better as APC for the stimulation of primary responses • Strong CTL responses were elicited by the epitopes DRFYKTLRA and GEIYKRWII when presented by either immature or mature dendritic cells – macrophages were not able to prime a CTL response against DRFYKTLRA • A weak response to KLTPLCVSL was stimulated using macrophages as the APC • No detectable response was observed for the following previously-defined HIV epitopes: KIRLRPGGK, ILKEPVHGV, IRLRPGGK, GPKVKQWPL				
p17 (18–26)	Gag (18–26)	KIRLRPGGK	HIV-1 infection	human (A3)	Brodie1999
	• The ability of CTL effector cells was studied by expanding autologous HIV-1 Gag-specific CTL in vitro, and adoptive transfer				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The transferred CTLs migrated to the lymph nodes and transiently reduced circulating productively-infected CD4+ T cells, showing that CTL move to appropriate target sites and mediate anti-viral effects				
p17 (18–26)	(18–26)	KIRLRPGGK	HIV-1 infection	human (A3)	Brodie2000
	• Study tracks and quantifies *in vivo* migration of neo-marked CD8 HIV-specific CTL • Adoptively transferred gene-marked HIV-specific CTL homed to specific lymph node sites, colocalizing within the parafollicular regions of the lymph node adjacent to cells expressing HIV tat-fusion transcripts, indicative of viral replication • The CTL clones expressed CCR5 and localized among HIV-1 infected cells expressing MIP-1alpha and MIP-1beta, CC-chemokines produced at sites of viral replication, suggesting a possible homing mechanism • This study provides a methodology for tracking and studying antigen specific CTL *in vivo*				
p17 (18–26)	p17 (18–26 IIIB)	KIRLRPGGK	HIV-1 infection	SJL/J HLA transgenic mice (A3)	Wilson1999a
	• This study describes maternal CTL responses in the context of mother-to-infant transmission • Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants • KIRLRPGGR and RIRLRPGGR were escape mutants • This epitope was recognized and many escape mutants were detected in an HLA A3 transmitting mother, and was recognized but invariant in an HLA A3 non-transmitting mother				
p17 (18–26)	p17 (18–26 IIIB)	KIRLRPGGK	HIV-1 infection	human (A3)	Goulder1997e, Goulder1997a
	• Identical twin hemophiliac brothers were both infected with the same batch of factor VIII. One had a response to this epitope, the other did not. [Goulder1997e] is a review of immune escape that summarizes this study.				
p17 (18–26)	p17 (subtype B)	KIRLRPGGK	HIV-1 exposed seronegative	human (A3)	Kaul2000
	• 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 gamma-IFN responses in the cervix – systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses • Low risk individuals did not have such CD8+ cells • CD8+ T cell epitopes: DTVLEDINL (3 individuals), SLYNVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women				
p17 (18–26)	p17 (SF2)	KIRLRPGGK	HIV-1 infection	human (A3)	Goulder2000a
	• WEKIRLRPGGKKKYKLK was the target of the dominant response in Caucasoids (38%) more frequently than non-Caucasoids (12%) – 7/10 that had a dominant response to this epitope were A3, and 5/7 targeted RLRPGGKKK while 2/7 targeted KIRLRPGGK • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK(p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa				
p17 (18–26)	p17	KIRLRPGGK	HIV-1 infection	human (A3)	Seth2001
	• CTL responses were studied by tetramer staining in 41 patients with combination therapy – activated CD8+ T-cells decline as the viral load drops in response to therapy, but the overall level of antigen-specific cells capable of differentiating into effectors stays constant and new epitopes may be recognized				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17 (18–26)	p17 (18–26 SF2)	KIRLRPGGK	HIV-1 infection	human (A3)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-A3+ individuals that had a CTL response to this epitope broken down by group: 3/7 group 1, 0/4 group 2, and 2/2 group 3				
p17 (18–26)	p17 (18–26)	KIRLRPGGK	HIV-1 infection, HIV-1 exposed seronegative	human (A3)	Kaul2001a
	• KIRLRPGGK is cross-reactive for A, B, and D clades • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers				
p17 (18–26)	p17 (JRCSF)	KIRLRPGGK	HIV-1 infection	human (A3)	Severino2000
	• Primary HLA-A3+ CD4+ and HLA-mismatched lymphocytes from uninfected donors were infected with JRCSF after isolation then cocultured with the A3-restricted CTL clone 11504/A7 specific for KIRLRPGGK, and viral inhibition was MHC-restricted • Primary monocytes and monocyte-derived DC were generated from the same donors, replication of HIV-1 in these cell types was less efficient than in lymphocytes and could also be inhibited by MHC-restricted CTL • DC-lymphocyte cluster cultures allowed vigorous viral replication and MHC-restricted CTL viral inhibition was blunted or lost depending on the ratio of DC to CD4+ lymphocyte in the culture				
p17 (18–26)	p17 (18–26)	KIRLRPGGK	HIV-1 infection	human (A3)	Day2001
	• The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person • All patients recognized at least 1 A3 epitope, up to 8 A3 epitopes, but none was clearly dominant				
p17 (18–26)	p17	KIRLRPGGK	HIV-1 infection	human (A3)	Ostrowski2000
	• The role of CD4+ T-cell help in expansion of virus-specific memory CTL was studied through co-culture *ex vivo* • Optimal expansion of HIV-1-specific memory CTL depended on CD4+ T cell help in 9 of 10 patients – CD40 ligand trimer (CD40LT) could enhance CTL in the absence of CD4+ T cell help to a variable degree in most of patients • Those CTL that didn't respond to CD40LT could expand with IL2 present, and IL15 produced by dendritic cells also contributes • The T-helper epitope used for CD4+ T cell stimulation was the universal tetanus helper epitope TET830-843 (QYIKANSKFIGITE)				
p17 (18–26)	Gag (p17) (18–26)	KIRLRPGGK	HIV-1 infection	human (A3)	Yu2002a
	• Epitope name: A3-KK9 • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06 was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• 8/14 HLA-A3 positive individuals had detectable A3-restricted responses during acute infection. Only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 7/8 individuals with acute responses had specific responses for this epitope. • KIRLRPGGK and RLRPGGKKK were the most commonly recognized HLA-A3 epitopes during acute infection, after 1 year of treatment, and after STI. RLRPGGKKK was immunodominant.				
p17 (18–26)	p17 (18–26)	KIRLRPGGK	HIV-1 infection	human (A3, A3.1, B27)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
p17 (18–26)		KIRLRPGGK	HIV-1 infection	human (B*0301)	Wilson2000a
	• Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load was also found • All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39 • ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK • The subject with A*0201 had a moderatly strong response to SLYNTVATL • Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705 • No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL			
p17 (18–27)	p17 (18–27 LAI)	KIRLRPGGKK		human (B27)	Brander1996b
	• D. Lewinsohn, pers. comm.				
p17 (18–27)	p17 (18–27)	KIRLRPGGKK	HIV-1 infection	human (B27)	Birk1998b
	• A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs				
p17 (18–31)	p17 (18–31)	KIRLRPGGKKKYKL	HIV-1 infection	human (A3)	Birk1998b
	• A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs				
p17 (18–31)	p17 (18–31)	KIRLRPGGKKKYKL	HIV-1 infection	human (B62)	Lubaki1997
	• Eighty two HIV-1-specific CTL clones from 5 long-term non-progressors were isolated and analyzed for breadth of CTL response • A sustained Gag, Env and Nef response was observed, and clones were restricted by multiple HLA epitopes, indicating a polyclonal response • A subject who was HLA-B62+ had CTL that recognized this peptide, and p24 LGLNKIVRMYS, and one additional unknown epitope				
p17 (18–42)	p17 (18–42 IIIB)	KIRLRPGGKKKYKLKHIVW-ASRELE	HIV-1 infection	human (A3)	Jassoy1992
	• Epitope recognized by CTL clone derived from CSF				
p17 (18–42)	p17 (18–42 PV22)	KIRLRPGGKKKYKLKHIVW-ASRELE	HIV-1 infection	human (A3)	Jassoy1993
	• HIV-1 specific CTLs release γ-IFN, and α- and β-TNF				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17 (18–42)	p17 (18–42 BH10)	KIRLRPGGKKKYKLKHIVW-ASRELE	HIV-1 infection	human (Bw62)	Johnson1991
	• Gag CTL response was studied in three individuals				
p17 (19–27)	p17 (19–27 JRCSF)	IRLRPGGKK	HIV-1 infection	scid-hu mouse (B*2705)	Brander2001
	• Noted by Brander to be B*2705 (Pers. Comm. D. Lewinsohn)				
p17 (19–27)	p17 (19–27 LAI)	IRLRPGGKK		human (B27)	Brander1996b
p17 (19–27)	p17 (19–27 JRCSF)	IRLRPGGKK	HIV-1 infection	scid-hu mouse (B27)	McKinney1999
	• Epitope-specific CTL were infused in infected human PBL-SCID mice, and transient decreases in viral load were observed, however virus was not eradicated and the HIV-specific CTL rapidly disappeared • No escape mutants were observed • Control CTL were long lived in both infected and uninfected mice, showing the rapid loss of CTL was due to target interaction				
p17 (19–27)	p17 (SF2)	IRLRPGGKK	HIV-1 infection	human (B27)	Goulder2000a
	• WEKIRLRPGGKKKYKLK was the target of the dominant response in Caucasoids (38%) more frequently than non-Caucasoids (12%) – 2/3 individuals that were B27+ had a dominant response to this epitope • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK(p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa				
p17 (19–27)	p17 (19–27)	IRLRPGGKK	HIV-1 infection	human (B27)	Day2001
p17 (19–27)	p17 (19–27)	IRLRPGGKK	HIV-1 infection	human (B27)	Goulder2001b
	• Epitope name: IK9 • This B27 epitope is generally recognized only if there is escape in the B27 dominant epitope, p24 KRWIILGLNK				
p17 (20–28)	p17 (20–28)	RLRPGGKKK	HIV-1 infection	human	Betts2000
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes • Three of the four individuals that responded to SLYNTVATL recognized HIV epitopes, and one individual who was A*0201, A31 and B51 and B58w4 recognized this epitope (previously described as HLA A3.1), as well as one other				
p17 (20–28)	p17 (20–28)	RLRPGGKKK	HIV-1 infection	human (A*03)	Goulder1997e, Goulder1997a
	• Identical twin hemophiliac brothers were both infected with the same batch of factor VIII • One had a response to gag A3 epitope RLRPGGKKK, the other non-responder carried the sequence RLRPGGKKC • [Goulder1997a] is a review of immune escape that summarizes this study				
p17 (20–28)	p17 (20–28)	RLRPGGKKK	HIV-1 infection	human (A*0301)	Brander2001
	• C. Brander notes that this is an A*0301				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17 (20–28)	p17	RLRPGGKKK	HIV-1 infection	human (A*0301)	Wilson2000a
	• Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load was also found • All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39 • ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK • The subject with A*0201 had a moderatly strong response to SLYNTVATL • Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705 • No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL			
p17 (20–28)	p17 (20–28 SF2)	RLRPGGKKK	HIV-1 infection	human (A*0301)	Altfeld2001a
	• HIV+ individual AC-06 was tested for reactive overlapping peptides spanning all HIV-1 proteins in an ELISPOT and was found to react with 12 peptides from 7 proteins, suggesting that the breadth of CTL responses are underestimated if accessory proteins are not included in the study • The reactive peptide p17 gag WEKIRLRPGGKKKYK contained two A*0301-restricted epitopes, KIRLRPGGK and RLRPGGKKK A*0301				
p17 (20–28)	Gag (p17) (20–28)	RLRPGGKKK	HIV-1 infection	human (A*0301)	Sabbaj2002a
	• Epitope name: RK9 • IFNgamma T-cell responses in breast milk of 5 HIV-1 infected women from the US and 6 from Zambia were tested with using Elispot. 11/11 women responded to Gag, 8/11 responded to Pol, 7/11 women to Nef, and 2/5 women to Env peptide pools. These responses were shown to be primarily due to CD8+ T-cells in one woman, and another woman had cytolytic responses measured by Cr-release. • Tetramer analysis of breast milk and peripheral blood samples of one volunteer showed responses to RLRPGGKKK in both compartments, 0.65% of CD3+/CD8+ cells in breast milk, and 0.22% of CD3+/CD8+ cells in peripheral blood cells. • The frequencies of responses in the two compartments differed, and 2/4 women that responded to epitopes in Nef 101-205 and Pol 601-710 showed responses in breast milk but no detectable responses in peripheral blood cells.				
p17 (20–28)		RLRPGGKKK	HIV-1 infection	human (A03)	Sabbaj2002b
	• Epitope name: Gag-RK9 • Among HIV+ individuals who carried HLA A03, 7/20 (35%) recognized this epitope				
p17 (20–28)	p17 (20–28)	RLRPGGKKK	HIV-1 infection	human (A3)	Goulder2000c
	• Two clonal CTL responses were generated in donor 021-BMC (HLA A3/3001, B42/-, Cw17/-) against different optimal versions of this epitope, one nine amino acids long, one ten • A previously described optimal A3 epitope overlapping this region, KIRLRPGGK, was not recognized by CTL from 021-BMC				
p17 (20–28)	p17 (20–28)	RLRPGGKKK	HIV-1 infection	human (A3)	Goulder1997f
	• A control CTL line that reacts with this peptide was included in the study				
p17 (20–28)	p17 (20–28)	RLRPGGKKK	HIV-1 infection	human (A3)	Cao1997a
	• The consensus peptide of A, B, and D clade viruses is RLRPGGKKK • The consensus peptide of C clade viruses is RLRPGGKKH and is equally reactive				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17 (20–28)	p17 (SF2)	RLRPGGKKK	HIV-1 infection	human (A3)	Goulder2000a
	• WEKIRLRPGGKKKYKLK was the target of the dominant response in Caucasoids (38%) more frequently than non-Caucasoids (12%) – 7/10 that had a dominant response to this epitope were A3, and 5/7 targeted RLRPGGKKK while 2/7 targeted KIRLRPGGK • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK(p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa			
p17 (20–28)	p17 (20–28 SF2)	RLRPGGKKK	HIV-1 infection	human (A3)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-A3+ individuals that had a CTL response to this epitope broken down by group: 5/7 group 1, 2/4 group 2, and 2/2 group 3			
p17 (20–28)	p17 (20–28)	RLRPGGKKK	HIV-1 infection	human (A3)	Day2001
	• The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person • All patients recognized at least 1 A3 epitope, up to 8 A3 epitopes, but none was clearly dominant				
p17 (20–28)	p17 (20–28)	RLRPGGKKK	HIV-1 infection	human (A3)	Goulder2001b
	• Epitope name: RK9 • Responses to this dominant A3-restricted Gag epitope are present during the time of decreasing viral load in acute infection • Mutations in this epitope were observed in autologous clones of subjects who were A3-positive with a higher frequency than those who were A3-negative (P = 0.0002) • These mutations are being sexually transmitted in adult infections				
p17 (20–28)	Gag (p17) (20–28)	RLRPGGKKK	HIV-1 infection	human (A3)	Yu2002a
	• Epitope name: A3-RK9 • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06 was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 8/14 HLA-A3 positive individuals had detectable A3-restricted responses during acute infection. Only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 7/8 individuals with acute responses had specific responses for this epitope. • KIRLRPGGK and RLRPGGKKK were the most commonly recognized HLA-A3 epitopes during acute infection, after 1 year of treatment, and after STI. RLRPGGKKK was immunodominant during acute infection and throughout the study period in the 5/6 individuals who targeted it.			

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17 (20–28)	Gag (LAI)	RLRPGGKKK	HIV-1 infection	human (A3)	Lewinsohn2002
	• CTL kill targets through releasing perforin, that forms pore in the plasma membrane, and granzymes, that induce apoptosis. • Vpr is capable of arresting infected cells in the G2 phase, and it was hypothesized that Vpr may inhibit CTL-mediated apoptosis because it interacts with the granzyme B molecular complex. • Vpr expression in the target cell did not inhibit epitope specific lysis – neither perforin or granzyme mediated events were inhibited, as measured by a Chromium release assay and a TUNEL assay. • In contrast, deletion of Nef, which is thought to protect primary HIV infected cells by down-regulating cell-surface expression of MHC class I complexes, increased the susceptibility of HIV-1 infected cells to CTL mediated killing 2-fold using the TUNEL assay				
p17 (20–28)	p17	RLRPGGKKK	HIV-1 infection	human (A3)	Sabbaj2002a
	• IFNgamma T-cell responses in breast milk of 5 HIV-1 infected women from the US and 6 from Zambia were tested with using Elispot. 11/11 women responded to Gag, 8/11 responded to Pol, 7/11 women to Nef, and 2/5 women to Env peptide pools. These responses were shown to be primarily due to CD8+ T-cells in one woman, and another woman had cytolytic responses measured by Cr-release. • T-cells in breast milk from a volunteer who was HLA A3, A11, B35, B51 induced IFNgamma after stimulation with a peptide that carries known A3 epitope RLRPGGKKK. • The frequencies of responses in the two compartments differed, and 2/4 women that responded to epitopes in Nef 101-205 and Pol 601-710 showed responses in breast milk but no detectable responses in peripheral blood cells.				
p17 (20–29)	p17 (20–29 LAI)	RLRPGGKKKY	HIV-1 infection	human (A*0301)	Brander2001
	• C. Brander notes this is an A*0301 epitope				
p17 (20–29)	p17 (20–29)	RLRPGGKKKY	HIV-1 infection	human (A3)	Goulder2000c
	• Two clonal CTL responses were generated in donor 021-BMC (HLA A3/3001, B42/-, Cw17/-) against different optimal versions of this epitope, one nine amino acids long, one ten • A previously described optimal A3 epitope overlapping this region, KIRLRPGGK, was not recognized by CTL from 021-BMC				
p17 (20–29)	p17 (20–29)	RLRPGGKKKY	HIV-1 infection	human (A3.1)	Brander1995b
	• Unpublished, C. Jassoy and Beatrice Culman, pers. comm.				
p17 (20–29)	p17 (20–29 LAI)	RLRPGGKKKY	HIV-1 infection	human (A3.1)	Wilkens1999
	• Pers. comm., B. Wilkens and D. Ruhl				
p17 (20–29)	p17 (20–29)	RLRPGGKKKY	HIV-1 infection	human (A30, A3.1)	Betts2000
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes • 1/11 of the A2+ individuals was A30, and one was A3, and both responded to RLRPGGKKKY • The A2+ A3 individual also reacted with two other A3.1 epitopes				
p17 (20–29)	p17 (20–29 IIIB)	RLRPGGKKKY	HIV-1 infection	human (B42)	Wilson1996
	• Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study • RLRPGGKKRY, a naturally occurring variant, was found in non-transmitting mother and is recognized • Binds HLA-A3 and Bw62 as well				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17 (20–29)	p17 (20–29)	RLRPGGKKKY	HIV-1 infection	human (B42, Bw62)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
p17 (20–29)	p17 (20–29)	RLRPGGKKKY	HIV-1 infection	human (B62)	Brodie2000
	• Study tracks and quantifies *in vivo* migration of neo-marked CD8 HIV-specific CTL • Adoptively transferred gene-marked HIV-specific CTL homed to specific lymph node sites, colocalizing within the parafollicular regions of the lymph node adjacent to cells expressing HIV tat-fusion transcripts, indicative of viral replication • The CTL clones expressed CCR5 and localized among HIV-1 infected cells expressing MIP-1alpha and MIP-1beta, CC-chemokines produced at sites of viral replication, suggesting a possible homing mechanism • This study provides a methodology for tracking and studying antigen specific CTL *in vivo*				
p17 (20–29)	p17 (20–29 LAI)	RLRPGGKKKY		human (Bw62)	McMichael1994
	• Review of HIV CTL epitopes • Also P. Johnson, pers. comm.				
p17 (20–30)	p17 (SF2)	RLRPGGKKKYK	HIV-1 infection	human	Goulder2000a
	• WEKIRLRPGGKKKYKLK was the target of the dominant response in Caucasoids (38%) more frequently than non-Caucasoids (12%) – the dominant response in a Haitian immigrant living in Boston who was HLA A24/29 B7/B44 Cw6/7 was to this epitope, although the restricting element was not determined • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK(p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa				
p17 (20–35)	p17 (90–105 SF2)	CLRPGGKKKYKLKHIV	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag • One of these 12 had CTL response to this peptide • The responding subject was HLA A-2, A-24, B-13, B-35				
p17 (21–35)	Gag	LRPGGKKKYKLKHIV	HIV-1 infection	human	Weekes1999a
	• Peptide 703.3: Memory CTL specific for HIV-1 may contribute to oligoclonal expansions within the CD57+ CD28- CD8+ CTLp populations				
p17 (21–35)	p17 (91–105 SF2)	LRPGGKKKYKLKHIV	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag • One of these 12 had CTL response to this peptide • The responding subject was HLA-A1, A2, B50, B57				
p17 (21–35)	Gag	LRPGGKKKYKLKHIV	HIV-1 infection	human (A3)	Weekes1999b
	• Peptide 703.3: Almost all CD8+ T cells are CD28+ at birth, and the proportion of CD28-CD8+ cells increases with age – this study examines the contribution of CD8+CD28- cells to CTL memory pools for CTL clones specific for two persistent human viruses, CMV and HIV – clones were found to be similarly distributed in the CD28 depleted cell population				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• HIV CTL responses to 3 Env and 2 Gag peptides were studied • The clonal composition of the TCR Vbeta responses was studied and was found to be highly focused, with one TCR beta-chain sequence tending to dominate the peptide-specific response – clones to this epitope were Vbeta13.1 and Vbeta5.2				
p17 (21–35)	p17 (21–35)	LRPGGKKKYKLKHIV		human (B8)	Nixon1991
	• Two CTL epitopes defined (see also p24(191-205))				
p17 (21–35)	p17 (21–35)	LRPGGKKKYKLKHIV	HIV-1 infection	human (not B8)	vanBaalen1996
	• Unknown HLA specificity, but not B8				
p17 (21–40)	p17 (21–40 subtype A)	LRPGGKKKYRLKHLVWASRE	HIV-1 infection	human (Cw4)	Dorrell1999
	• CTL responses in three individuals with non-clade B infections were studied, 2 with subtype A infections, 1 with subtype C – their infections all originated in East Africa • This epitope was defined in an A subtype infection – the B clade variant (LRPGGKKKYKLKHIVWASRE) has two mutations relative to the A subtype form, and the CTL from this patient were not A-B cross-reactive				
p17 (22–31)	Gag (22–31)	RPGGKKRYKL	HIV-1 infection	human (B7)	Jin2000b
	• This B7 epitope is one of three subdominant CTL responses detected in a long-term non-progressor • A dominant B7 epitope was defined using conventional methods, and three additional sub-dominant HLA B7 epitopes were defined by first using a non-anchor based strategy, EpiMatrix, to identify 2078 possible epitopes in the autologous HIV-1, followed by B7 anchor residue prediction to narrow the set to 55 peptides for experimental testing				
p17 (24–31)	p17 (24–31)	GGKKKYKL		human (B8)	Goulder1997g
	• The crystal structure of this peptide bound to HLA-B8 was used to predict new epitopes and the consequences of epitope variation • The predictions were experimentally confirmed • The anchors for HLA-B8 epitopes, as defined by peptide elution data, are P3 (K), P5 (K/R), and P8 (L) • Structural data suggests that a positive charge at P5 is essential, but that the constraints on P3 may be less severe • Small hydrophobic residues at P2 may be favorable for binding • A spacious F-pocket favors mid-sized hydrophobic residues in the C-term anchor				
p17 (24–31)	p17 (24–31 SF2)	GGKKKYKL	HIV-1 infection	human (B8)	McAdam1998
	• CTL from a patient infected with clade B virus did not recognize Ugandan variants of this epitope				
p17 (24–31)	p17 (24–31 LAI)	GGKKKYKL	HIV-1 infection	human (B8)	Reid1996
	• The variants 7R: GGKKKYRL, 7Q: GGKKKYQL, 5R: GGKKRYKL, and 3R: GGRKKYKL, were studied • Crystal structures were obtained to study these peptides in the context of HLA-B8, and CTL binding and activity were determined • 3R has been detected in 3 patients, and it abolishes recognition causing extensive conformational changes upon binding including MHC main chain movement • 7Q and 7R alter the TCR exposed surface, and retain some recognition • Reactivity of 5R depends on the T cell clone, this amino acid is embedded in the C pocket of B8 when the peptide is bound • Optimal peptide is 8-mer, not 9-mer, and positions 3, 5, and 8 are the anchor residues				
p17 (24–31)	p17 (24–31 LAI)	GGKKKYKL	HIV-1 infection	human (B8)	Price1997
	• A weak CTL response to the index peptide was observed in an HLA-B8+ infected individual • Sequences from the earliest available time point showed that a variant at position 5, an anchor residue, GGKKQYKL, was present				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17 (24–31)	p17 (24–31 SF2)	GGKKKYKL	HIV-1 infection	human (B8)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-B8+ individuals that had a CTL response to this epitope broken down by group: 0/3 group 1, 1/3 group 2, and 2/2 group 3			
p17 (24–31)	p17 (24–31)	GGKKKYRL	HIV-1 infection, HIV-1 exposed seronegative	human (B8)	Kaul2001a
	• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers				
p17 (24–31)	p17 (24–31)	GGKKKYKL	HIV-1 infection	human (B8)	Day2001
	• B8-restricted CTL accounted for about 1/3 of the total CTL response in one individual				
p17 (24–31)	p17	GGKKKYKL	HIV-1 infection	human (B8)	McMichael2002
	• CTL response-eliciting vaccines are reviewed. The natural epitope interactions with the HLA class I presenting molecules and T-cell receptors are described, using the structure of this epitope, taken from [Reid1996], as an example.				
p17 (24–32)	p17 (24–32 LAI)	GGKKKYKLK	HIV-1 infection	human (B*0801)	Brander2001
	• C. Brander notes epitope to be presented by B*0801				
p17 (24–32)	p17 (24–32 LAI)	GGKKKYKLK	HIV-1 infection	human (B8)	Sutton1993
	• Exploration of HLA-B8 binding motif through peptide elution				
p17 (24–32)	p17 (24–32 LAI)	GGKKKYKLK	HIV-1 infection	human (B8)	Rowland-Jones1993
	• Study of an individual with partially defective antigen processing				
p17 (24–32)	p17 (24–32)	GGKKKYKLK	HIV-1 infection	human (B8)	Klenerman1994
	• Naturally occurring variants GGKKKYQLK and GGKKRYRLK may act as antagonists				
p17 (24–32)	p17 (24–32)	GGKKKYKLK	HIV-1 infection	human (B8)	Klenerman1995
	• Naturally occurring antagonist GGKKKYQLK found in viral PBMC DNA and RNA				
p17 (24–32)	p17 (24–32)	GGKKKYKLK	HIV-1 infection	human (B8)	Nowak1995
	• Longitudinal study of CTL response and immune escape – the variant GGRKKYKLK binds to HLA-B8 but is not reactive				
p17 (24–32)	p17 (24–32)	GGKKKYKLK	HIV-1 infection	human (B8)	Dyer1999
	• CTL specific responses were measured over a 1.3 to 1.5 year period in members of the Sydney Blood Bank Cohort (SBBC) who had been infected with a natural attenuated strain of HIV-1 which was Nef-defective • Some of these patients had prolonged high levels of CTL effector and memory cells despite low viral load				
p17 (24–32)	p17	GGKKKYKLK		human (B8)	Rowland-Jones1999
	• CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, and the B35 allele seems to be protective • HIV-2 sequence: GGKKKYKMK – no cross-reactivity [Phillips1991]				
p17 (24–32)	p17 (24–32)	GGKKKKYKLK	HIV-1 infection	human (B8)	Oxenius2000
	• Epitope name: GGK • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable • This epitope was recognized by 1/7 study subjects that were HLA-B8+ • Patient SC12(HLA A1, B8/39, Cw0701/0702, DR2/3, DR51/52, DQ2/6) had sustained therapy started during acute infection and maintained an immunodominant response to FLKEKGGL throughout and minor responses to GEIYKRWII, DCKTILKAL, GGKKKYKLK – GEIYKRWII and GGKKKYKLK responses were stimulated by a brief period off therapy			
p17 (24–32)	p17	GGKKKKYKKL	HIV-1 infection	human (B8)	Seth2001
	• CTL responses were studied by tetramer staining in 41 patients with combination therapy – activated CD8+ T-cells decline as the viral load drops in response to therapy, but the overall level of antigen-specific cells capable of differentiating into effectors stays constant and new epitopes may be recognized				
p17 (24–32)	p17	GGKKKKYKLK	HIV-1 infection	human (B8)	Oxenius2002b
	• Epitope name: GGK • Using previously defined epitopes [Oxenius2000, Oxenius2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI). • STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.				
p17 (24–35)	p17 (25–35 SF2)	GGKKKYKLKHIV	HIV-1 infection	human (B8)	Goulder1997a, Phillips1991
	• Longitudinal study of CTL escape mutants in people with the appropriate HLA types – little variation was observed in the immunodominant B27 epitope, relative to B8 epitopes, which varied over time • [Goulder1997a] is a review of immune escape that points out that there may be a protective effect associated with B27, and that HLA-B8 individuals tend to progress more rapidly than HLA B27 patients				
p17 (24–35)	p17 (25–35)	GGKKKYKLKHIV	HIV-1 infection	human (B8)	Birk1998b
	• A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs				
p17 (28–36)		KYRLKHLVW	HIV-1 infection	human	Kaul2001c
	• This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative • The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire • This epitope was recognized in 1/22 HEPS sex worker controls (ML1573)				
p17 (28–36)	p17 (28–36 LAI)	KYKLKHIVW		human (A*2402)	Brander2001
	• Ikeda-Moore(1998) and D. Lewinsohn, pers. comm.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• C. Brander notes that this is an A*2402 epitope				
p17 (28–36)	p17 (28–36 SF2)	KYKLKHIVW	HIV-1 infection	human (A*2402)	Ikeda-Moore1998
	• Strong CTL activity to this peptide was detected in 2/3 HIV-infected individuals who were HLA A24+ • HLA A24 is very common in Japanese (70% carry it) and is common globally • This epitope was detected by looking for peptides with appropriate A24 anchor residues (Y at position 2, carb-term ILF or W) – 16/17 such peptides bound to A24 – KYKLKHIVW was found to be a naturally processed epitope that elicits a strong CTL response.				
p17 (28–36)	p17 (28–36 LAI)	KYKLKHIVW		human (A23)	Goulder1999b
	• P. Goulder, pers. comm.				
p17 (28–36)	p17 (28–36 LAI)	KYKLKHIVW		human (A24)	Brander1996b
	• D. Lewinsohn, pers. comm.				
p17 (28–36)	p17 (28–36 SF2)	KYKLKHIVW	HIV-1 infection	human (A24)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-A24+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 2/3 group 2, and 0/0 group 3				
p17 (28–36)	p17 (28–36 93TH253 subtype CRF01)	KYKLKHIVW	HIV-1 infection	human (A24)	Bond2001
	• More than half of a cohort of HIV+ female sex workers (FSW) from Northern Thailand were HLA-A11 positive, and this study concentrated on A11 epitopes in this group, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested. • The only HLA-A24 FSWs tested did not recognized the E clade version of this epitope KYKMKHLVW, which differs from the previously defined B clade version by two amino acids, KYKLKHIVW				
p17 (28–36)	p17 (728–736 subtype A)	KYRLKHLVW	HIV-1 infection, HIV-1 exposed seronegative	human (Cw4)	Kaul2001a
	• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure • Among HLA-Cw4 women, 2/2 HEPS and 7/11 HIV-1 infected women recognized this epitope • The dominant response to this HLA allele was to this epitope in both of the 2/2 HEPS cases and in 3 of the 7/11 HIV-1 infected women				
p17 (28–36)	p17 (28–36)	KYRLKHLVW	HIV-1 infection	human (Cw4)	Appay2000
	• This epitope is newly defined in this study • Combined tetramer and intracellular cytokine staining was used to study the function of circulating CD8+ T cells specific for HIV and CMV				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• HIV-specific CD8+ T cells expressed lower levels of perforin than CMV-specific CD8+ T cells from the same donor, and this was associated with persistent CD27 expression on HIV-specific cells, suggesting impaired maturation • In most donors, between 50% and 95% of the activated virus-specific CD8+ T cells produced IFN-γ and MIP-1β with a distinct subset that failed to produce TNF-α				
p17 (36–44)	p17 (SF2)	WASRELERF	HIV-1 infection	human	Goulder2000a
	• The dominant response in an African American who was HLA A3/33 B35/B53 Cw4/7 was to this epitope, although the restricting element was not determined – this epitope fell outside the most recognized peptides in the study • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK(p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa				
p17 (36–44)	p17 (35–43 LAI)	WASRELERF	HIV-1 infection	human (B*3501)	Goulder1997d
	• Optimal epitope defined from within p17(30-44), LKHIVWASRELERFA • Dominant CTL response in an HIV+ asymptomatic donor was to this epitope • The Phe in the C-term anchor is distinct from the previously-defined Tyr for B*3501 C-term anchors				
p17 (36–44)	p17 (36–44 LAI)	WASRELERF		human (B*3501)	Brander2001, Goulder1997b
	• C. Brander notes this is a B*3501 epitope				
p17 (36–44)	p17 (36–44)	WASRELERF	HIV-1 infection	human (B35)	Birk1998b
	• A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs				
p17 (36–44)	p17 (36–44)	WASRELERF	HIV-1 infection	human (B35)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
p17 (36–44)	p17 (36–44 SF2)	WASRELERF	HIV-1 infection	human (B35)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-B35+ individuals that had a CTL response to this epitope broken down by group: 0/2 group 1, 0/2 group 2, and 1/1 group 3				
p17 (36–44)		WASRELERF	HIV-1 infection	human (B35)	Sabbaj2002b
	• Epitope name: Gag-WF9 • Among HIV+ individuals who carried HLA B35, 1/21 (5%) recognized this epitope				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17 (69–93)	p17 (69–93 BH10)	QTGSEELRSLYNTVATLYC-VHQRIE	HIV-1 infection	human (A2)	Johnson1991
	• Gag CTL response studied in three individuals				
p17 (71–79)	p17 (71–79 LAI)	GSEELRSLY		human (A1)	Brander1996b
	• P. Goulder, pers. comm.				
p17 (71–79)	p17 (71–79)	GSEELRSLY	HIV-1 infection	human (A1)	Birk1998b
	• A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs				
p17 (71–79)	p17 (71–79 HXB2)	GSEELRSLY	HIV-1 infection	human (A1)	Oxenius2000
	• Epitope name: GSE • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable • This epitope was not recognized by the 6/8 study subjects that were HLA-A1				
p17 (71–79)	p17 (71–79)	GSEELRSLY	HIV-1 infection, HIV-1 exposed seronegative	human (A1)	Kaul2001a
	• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure • Among HLA-A1 women, 1/1 HEPS and 3/3 HIV-1 infected women recognized this epitope, and the response was the dominant HLA-A1 response in all cases				
p17 (71–79)	p17	GSEELRSLY	HIV-1 infection	human (A1)	Oxenius2002b
	• Epitope name: GSE • Using previously defined epitopes [Oxenius2000, Oxenius2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI). • STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.				
p17 (71–85)	p17 (71–85 SF2)	GSEELRSLYNTVATL	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag • One of these 12 had CTL response to this peptide • The responding subject was HLA-A1, A11, B8, B27				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17 (74–82)	p17	ELRSLYNTV		human (B*0801)	Brander2001
	• Noted by Brander to be a B*0801 epitope				
p17 (74–82)	p17	ELRSLYNTV		human (B8)	Goulder1997g
	• Defined in a study of the B8 binding motif				
p17 (74–82)	p17 (74–82)	ELRSLYNTV	HIV-1 infection	human (B8)	Birk1998b
	• A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs				
p17 (74–82)	p17 (74–82)	ELRSLYNTV	HIV-1 infection	human (B8)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
p17 (74–82)	p17 (74–82)	ELRSLYNTV	HIV-1 infection	human (B8)	Day2001
	• B8-restricted CTL accounted for about 1/3 of the total CTL response in one individual				
p17 (76–86)	p17 (74–86 LAI)	RSLYNTVATLY		human (A*3002)	Brander2001
	• C. Brander notes this is an A*3002 epitope				
p17 (76–86)	p17 (SF2)	RSLYNTVATLY	HIV-1 infection	human (A*3002)	Goulder2000a
	• The CTL-dominant response was focused on this epitope in a single HIV+ individual from Boston – this epitope fell outside the most recognized peptides in the study • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK(p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa				
p17 (76–86)	Gag (96ZM651.8)	RLSYNTVATLY		human (A*3002)	Novitsky2001
	• This study is provides a survey of CTL responses and full length HIV-1 genome sequences from a C subtype infected Botswanan cohort • Only 3 of 13 (23.1%) A*3002-positive subjects demonstrated moderate CTL responses to the peptide GTEELRSLYNTVATLYCVHE (residues 71 to 90), which contains the previously described A*3002 epitope RLSYNTVATLY				
p17 (76–86)	p17 (76–86)	RSLYNTVATLY	HIV-1 infection	human (A*3002)	Goulder2001a
	• Epitope name: RY11 (p17) • HLA-A*3002 is very common in African populations, 50% of Zimbabweans express HLA-A30, 44% in African Zulu, so five new HIV epitopes were characterized that are presented by this HLA molecule • A rapid method was developed combining ELISPOT with intracellular IFN-γ staining of PBMCs to map optimal epitopes, then HLA presenting molecules were defined – this method was completed within 48 to 72 hours of receipt of blood • Two individuals were studied: Subject 199 (HLA A*0201/*3002 B*4402/51 Cw2/5), a Caucasian, and Subject 6007 (HLA A*3002/ B53/*5801 Cw4/7) an African-Caribbean • In both HLA-A*3002 individuals the response to RSLYNTVATLY was dominant • Three quantitative assays, ELISPOT, precursor frequency and chromium release, confirmed a hierarchy of response: RY11 (p17) > KY9 (gp41) > KY9 (RT-53) > IY9 (gp41)				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• HLA-A*3001-positive targets do not present RSLYNTVATLY				
p17 (76–86)		RSLYNTVATLY	HIV-1 infection	human (A*3002)	Sabbaj2002b
	• Epitope name: Gag-RY11 • This study monitored epitope responses in HIV-1 infected minority women living in the United States • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release • Subject 00RCH33 was on HAART had a viral load of 2900 and CD4 count of 727 and also recognized the epitopes YPLTFGWCY, Nef(135-143), HLA B*5301; AETFYVDGA, RT(437-445), HLA B*4501; and HIGPGRAFY, gp160(310-318), HLA A*3002 • Among HIV+ individuals who carried HLA B30, 3/16 (19%) recognized this epitope				
p17 (76–86)	p17 (74–86 SF2)	RSLYNTVATLY	HIV-1 infection	human (A30)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-A30+ individuals that had a CTL response to this epitope broken down by group: 0/1 group 1, 0/0 group 2, and 1/1 group 3				
p17 (76–86)	p17	RSLYNTVATLY	HIV-1 infection	human (A30)	Altfeld2002
	• Epitope name: A30-RY11(p17) • Peripheral blood (PB) and lymph node (LN) CD8+ T-cell responses were compared in 15 asymptomatic HIV-1 infected patients using all known optimal CTL epitopes (http://hiv-web.lanl.gov/content/hiv-db/REVIEWS/brander2001.html) for each person's class I HLA alleles. • 60 epitope responses were detected in both PB and LN samples of the 15 patients, and an additional 8 responses were detected only in LN. The total magnitude of the response was similar in LN and PB, but the percentage of CD8+ T cells in the LN is lower so the number of HIV-specific cells per million CD8+ T-cells is higher in the LN. • 1 year post-HAART treatment in five patients studied, the magnitude of the CD8 T-cell response was decreased in both LN and PB, but more dramatically in PB, and 13/25 epitope responses in the PB became undetectable, in contrast to 5/26 in the LN. • Treatment interruption following HAART induced resulted in increased viremia accompanied by the restoration of the detection of 13 epitopes that had become undetectable in the PB, and the addition of 9 novel epitope responses. • Breakdowns of epitope responses were shown for 4 individuals. Patient D displayed the greatest response to B27-KK10 (p24), and also responded to A30-RY11(p17), A32-PW10(RT), A30-KY11(RT), A32-RW10(gp120), and B18-YY9(Nef).				
p17 (77–85)	p17	SLYNTVATL	HIV-1 infection	human	Sewell2000
	• Review of the impact of CTL on viral immunity and escape that notes that SLYNTVATL-tetramer binding cells in individuals that react to this epitope inversely correlate with plasma viral load				
p17 (77–85)	(SF2, HXBc2/Bal chimeric)	SLYNTVATL	HIV-1 infection		Douek2002
	• Epitope name: SL9 • Seven HIV-positive subjects tended to make their strongest CD8+ T-cell response against Gag; these responses had varying breadth and magnitude that were unrelated to disease progression. • Patient TX7 primarily recognized SL9 during a three year study period and used six T-cell clonotypes for this recognition.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• SLYNTVATL was the only form of the epitope found initially, but three alternate forms eventually appeared: SLYNTVAVL, SLYNTIATL, and most commonly SLYNTIAVL. These distinct forms bind A2, but have distinct abilities to stimulate different T-cell clonotypes. • In subject TX7, the observed mutations of SL9 failed to escape overall CTL recognition, presumably because the six T-cell clonotypes allowed a more flexible response. • The BV17 T-cell clone recognized SL9 but not SLYNTIAVL, and BV17 became undetectable at week 20 when SLYNTIAVL predominated. Subsequently BV17 became the second most common clone. Thus the relative frequency of of the T-cell clonotypes varied with respect to each other and to epitope variation.				
p17 (77–85)	Gag p17 (77–85 LAI)	SLYNTVATL	HIV-1 infection	human	Luzuriaga2000
	• Longitudinal study of 8 infants with prolonged viral suppression due to combination antiretroviral therapy showed no HIV-1 specific CTL responses in peripheral blood cells. 6/8 were studied using a Chromium release assay and no response was detected using Gag expressed in vaccinia in the target cells. Three HLA-A*0201 children were tested using SLYNTVATL or ILKEPVHGV HLA A*0201 tetramers and again no HIV-specific response was detected, either using PBMC specimens, or PBMC which had been stimulated in vitro for a week. • In contrast, one of the children with therapy suppressed HIV viral replication who was co-infected with HIV and EBV, while HIV-tetramer negative, had EBV-tetramer staining cells at a frequency of 0.14% in the PBMC.				
p17 (77–85)	p17 (77–85)	SLYNTVATL	HIV-1 infection	human (A*02)	Huang2000
	• The single cell ELISPOT assay was optimized and highly specific, and found to work well even after the primary cells had been frozen and thawed • Increases in gamma IFN producing cells were observed in response to anti-retroviral therapy using single cell IFN-gamma-production ELISPOT • 4/8 A*02 subjects had a positive response to this epitope indicating that it is a major epitope for CD8+ gamma IFN production • In 3/3 HLA A*02, B*27 individuals, the dominant response in gag measured by both gamma IFN production and T cell lysis was a B27 epitope, p24(263-272), not the A2 SLYNTVATL epitope				
p17 (77–85)	p17 (77–85)	SLYNTVATL	HIV-1 infection	human (A*02)	Rinaldo2000
	• Epitope name: SL9 • Administration of triple-drug antiretroviral therapy (IDV, 3TC and ZDV) sometimes showed a transient increase and other times failed to increase CTL responses in patients with advanced HIV disease, but there is a stable population of tetramer stained HIV-specific CD8+ CD45RO+ cells that can persist after therapy and long periods of virus being below the level of detection				
p17 (77–85)	p17	SLYNTVATL	HIV-1 infection	human (A*02)	Scott-Algara2001
	• Epitope name: SL9 • This study examined with CTL response in HLA A*02+ children by tetramer staining for HLA-A2 immunodominant epitopes SLYNTVATL and ILKEPVHGV • 71% of the 28 HIV-1 infected HLA-A*02 positive children recognized both epitopes, with cells from 26 children stained positive by the gag tetramer (SLYNTVATL) and 21 children by the pol tetramer (ILKEPVHGV) • There were no differences observed in children that had therapy versus those that did not • Tetramer-binding cells were memory activated CD28-, CD45RO+, CD45RA- HLADR+, CD69-, CD8+ T-cells				
p17 (77–85)	p17 (77–85 HXB2)	SLYNTVATL	HIV-1 infection	human (A*0201)	Brander1999
	• Epitope name: SL9 • Multiple natural variations in the SL9 flanking regions of the immunodominant epitope SLYNTVATL were tested and found not to adversely affect CTL recognition or prevent epitope processing, suggesting that viral escape from the HLA-A*0201-restricted CTL response against SLYNTVATL is probably not linked to variations in the flanking regions of this epitope				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The substitution Y79F was an escape mutation in that it interfered with CTL recognition by one CTL clone from an A*0201 infected individual, clone 13010.B17, but it was still recognized by another CTL clone, 115.D4				
p17 (77–85)	Gag	SLYNTVATL	HIV-1 infection	human (A*0201)	Tan1999
	• Adoptive transfer of two autologous in vitro-expanded CTL clones against the A*0201 restricted epitopes SLYNTVATL and VIYQYMDDL were infused into a patient – they were well tolerated, but the SLYNTVATL clone was shown by tetramer staining to be rapidly eliminated through apoptosis, and the treatment had no impact upon viral load and CD4 and CD8 cell counts				
p17 (77–85)	p17 (77–85)	SLYNTVATL	HIV-1 infection	human (A*0201)	Betts2000
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes • Individuals that did not respond to SLYNTVATL recognized other HIV epitopes, and 2/4 SLYNTVATL responders had stronger responses to epitopes restricted by other class I alleles • SLYNTVATL was the only response detected in a one individual that was HLA A*0201, B44, B70				
p17 (77–85)	p17 (77–85)	SLYNTVATL	HIV-1 infection	human (A*0201)	Ogg1999
	• Epitope name: SL9 • CTL effector levels were measured after potent ARV therapy using HLA-tetramer complexes for the A*0201 epitopes SLYNTVATL and ILKEPVHGV in seven patients, and the B*3501 epitope DPNPQEVVL in one additional patient • Levels of CTL effectors typically decline for 5-7 days and then rebound, fluctuating during the first two weeks of therapy • After the early fluctuation, there was a steady exponential decay with a median half-life of 45 days				
p17 (77–85)	p17 (77–85)	SLYNTVATL	HIV-1 infection	human (A*0201)	Altman1996
	• Epitope name: SL9 • This paper introduces the tetramer methodology which permits quantification of specific CTL based on expression of specific TCRs – HLA-A2 tetramers were prepared that can stain CTL lines specific for ILKEPVHGV and SLYNTVATL, and quantitate HIV-specific CD8+ cell lines in freshly isolated PBMCs • Three patients only stained the Gag epitope SLYNTVATL, one patient had the highest frequency of tetramer staining to the Pol epitope (0.77%), less to the Gag epitope (0.28%)				
p17 (77–85)	Gag	SLYNTVATL	HIV-1 infection	human (A*0201)	Gray1999
	• Administration of highly active antiretroviral therapy (HAART) reduced CD8+ cell frequency, and the CD8+ cells detected by tetramer staining were likely to be memory cells, indicating that persistently replicating viral populations are needed to maintain high frequencies of HIV-1 specific CTL				
p17 (77–85)	p17 (77–85 SF2)	SLYNTVATL	HIV-1 infection	human (A*0201)	McAdam1998
	• Epitope name: SL9 • CTL from a patient infected with clade B virus did not recognize the clade A analog of this epitope				
p17 (77–85)	p17 (77–85)	SLYNTVATL	HIV-1 infection	human (A*0201)	Wilson1998a
	• Epitope name: SL9 • HIV+ individuals were followed longitudinally using MHC tetramers in combination with 14 anti-BV chain MAbs, and clonal expansion of HIV-specific T cells was followed in vivo • Seven HIV+ people were studied, and all showed expansions of particular TCR BV clones, often several, relative to uninfected controls • Three patients were followed in detail, TCR VB expansions persisted for 2 to 3 years, with occasional transient increases • An A2-Gag specific line from one patient was found to be BV8, and at its highest level represented 17.5% of the patient's CD8+ T cells				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17 (77–85)	p17 (77–85)	SLYNTVATL	HIV-1 infection	human (A*0201)	Ogg1998b
	• Epitope name: SL9 • HLA-tetrameric complexes were used in a cross-sectional study of 14 untreated HLA A*0201 positive individuals, revealing an inverse relationship between HIV Gag and Pol specific CTL effector cells (CTLe) and viral load • Inclusion of both the p17 SLYNTVATL and RT ILKEPVHGV epitopes gives a good representation of HLA A*0201-restricted activity • No correlation was observed between the CTLe and CD4 count or clearance rate of productively infected cells				
p17 (77–85)	p17 (77–85)	SLYNTVATL	in vitro stimulation	human (A*0201)	Walter1997
	• Epitope name: SL9 • HLA-A2 heavy chain and β2-microglobulin expressed in E. coli were refolded in the presence of this peptide • The HLA-A2-peptide complex elicited HLA-A2 peptide-specific CTL response in cells lacking HLA-A2 • Suggests that preformed HLA-peptide complexes could provide an alternate to intracellular processing for immunogens				
p17 (77–85)	p17 (77–85)	SLYNTVATL	HIV-1 infection	human (A*0201)	Lalvani1997
	• Epitope name: SL9 • A peptide-based protocol was optimized for restimulation of CTLp using optimized peptide and IL-7 concentrations – importantly this protocol does not stimulate a primary response, only secondary – peptide-specific CTLp counts could be obtained via staining with peptide-Class I tetramers • This peptide was one of the test peptides for optimizing the protocol				
p17 (77–85)	p17 (76–84)	SLYNTVATL	in vitro stimulation	human (A*0201)	vanderBurg1996
	• Epitope name: SL9 • Slow dissociation rate is associated with immunogenicity • CTL generated by in vitro stimulation of PBMC derived from uninfected individual				
p17 (77–85)	p17 (77–85)	SLYNTVATL	HIV-1 infection	human (A*0201)	Goulder1997e, Goulder1997a
	• Epitope name: SL9 • Identical twin hemophiliac brothers were both infected with the same batch of factor VIII • One had a response to gag A2 epitope SLYNTVATL, the other to pol A2 epitope ILKEPVHGV • Viral sequencing from the twin that had no response to SLYNTVATL indicated his virus had the substituted form SLHNAVAVL • 71% of an additional set of 22 HIV-1 infected HLA-A*0201 positive donors preferentially responded to gag SLYNTVATL • Those individuals with a pol ILKEPVHGV response tended to have mutations in or around SLYNTVATL • An additional subject went from SLYNTVATL responder to non-responder coincident with a switch to the variant SLFNTVATL • [Goulder1997a] is a review of immune escape that summarizes this study				
p17 (77–85)	Gag (77–85)	SLYNTVATL	HIV-1 infection	human (A*0201)	Gray1999
	• Epitope name: SL9 • Peptide-tetramer complexes of A*0201 and SLYNTVATL or ILKEPVHGV were used to study individuals receiving HAART to determine the frequency of Class I HLA-restricted anti-HIV CD8+ T cells • 17/18 asymptomatic patients had a CTL response to one or both epitopes – 72% had a CTL response to SLYNTVATL • After HAART, the majority of the epitope-specific CTL were apparently memory cells				
p17 (77–85)	p17 (77–85 subtype A)	SLFNTVATL	HIV-1 infection	human (A*0201)	Dorrell1999
	• Epitope name: SL9 • CTL responses in three individuals with non-clade B infections were studied, 2 with subtype A infections, 1 with subtype C – their infections all originated in East Africa				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This epitope is most commonly SLYNTVATL in B subtype, and CTL from the C subtype infection did not recognize B clade gag or the 3Y form of the epitope, but do recognize the predominant A and C clade form, SLFNTVATL				
p17 (77–85)	p17 (77–85)	SLYNTVATL	HIV-1 infection	human (A*0201)	Brander1998a
	• Epitope name: SL9 • Of 17 infected HLA A*0201 subjects, 13 had CTL responses against the p17 SLYNTVATL epitope, six recognized ILKEPVHGV and five recognized VIYQYMDDL, and there was no correlation between viral load and recognition of a specific epitope • Only one subject had CTL against all three epitopes • There was significant heterogeneity in the CTL response to this immunodominant epitope • The overall variation in this epitope among the 17 who had a CTL response and 11 non-HLA A*0201 HIV-1+ individuals was similar, suggesting a lack of immune pressure • Subjects were part of the San Francisco City Clinic Cohort, the ARIEL project and from the Boston area				
p17 (77–85)	p17 (77–85 HXB2)	SLYNTVATL	HIV-1 infection	human (A*0201)	Hay1999b
	• Epitope name: SL9 • CTL response to IPRRIRQGL was the immunodominant response in a rapid progressor – there was a subdominant response to SPAIFQSSM in Pol, and interestingly, no response to commonly immunodominant HLA A*0201 epitope SLYNTVATL, although this individual was HLA A*0201 • The individual showed a strong initial CTL response at the time of the initial drop in viremia, but it was quickly lost, although memory cells persisted • Despite the initial narrow response to two epitopes, no other CTL responses developed • No HIV-specific lymphoproliferative responses were detected in this patient, and neutralizing antibody response was weak • A variant of this epitope was observed in vivo (–F—-V-), but this mutation is recognized by SLYNTVATL-specific CTL, and in this case the patient's cells could present the peptide to SLYNTVATL-specific CTL				
p17 (77–85)	p17 (77–85)	SLYNTVATL	HIV-1 infection	human (A*0201)	Kalams1999b
	• Two patients were followed before and after HAART – reduced plasma HIV-1 RNA levels resulted in a decline in HIV-specific in-vivo activated CTL such that by day 260 CTL activities were undetectable • ERYLKDQQL was the dominant response in one of the individuals, SLYNTVATL subdominant • Sporadic breakthrough in viremia resulted in transient increases in CTLp • Memory CTL frequency directed against Vac-Gag, Vac-RT, Vac-Env, and Vac-Nef initially increased with HAART and then decreased with the decline of the viral load				
p17 (77–85)	Gag (77–85)	SLYNTVATL	HIV-1 infection	human (A*0201)	Spiegel2000
	• High levels of CD8+ HIV-1 specific and cytomegalovirus specific CTL were detected by HLA-A*0201-peptide tetramers in 3 infected subjects with very low CD4 counts, but CD8 T cell mediated effector activity was not seen • Thus HIV-1 specific CD8+ cells may be present but may lack direct effector activity in late disease, suggesting that overcoming antigen unresponsiveness may be a useful therapeutic strategy				
p17 (77–85)	Gag (77–85)	SLYNTVATL	HIV-1 infection	human (A*0201)	Larsson1999
	• ELISPOT was used to assay the CD8 T cell response to the HIV-1 proteins Gag, Pol, Nef or Env expressed in vaccinia vectors in 19 HIV+ people • The highest CTL frequency was directed at epitopes Pol • In A*0201 individuals, higher numbers of spot-forming T cells were directed against HIV-1 proteins expressed in vaccinia than to peptides SLYNTVATL and ILKEPVHGV presented by A2				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17 (77–85)	p17 (SF2)	SLYNTVATL	HIV-1 infection	human (A*0201)	Goulder2000a
	• The CTL-dominant response was focused on this epitope in 11/25 HLA A2 (A*0201 or A*0202) HIV+ individuals from Boston and in 1/8 HLA A2 HIV+ individuals from Durban • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK(p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa			
p17 (77–85)	p17 (77–85 LAI)	SLYNTVATL		human (A*0201)	Brander2001
	• C. Brander notes this is an A*0201 epitope				
p17 (77–85)	p17 (77–85 SF2)	SLYNTVATL	HIV-1 infection	human (A*0201)	Goulder2001a
	• Epitope name: SL9 • This epitope is targeted by 75% of HLA-A*0201, HIV+ adults, and the magnitude of the response is inversely correlated with viral load • CTL responses to SL9 and autologous SL9 variants were not detected in 11 HLA-A*0201 positive subjects during acute infection • Longitudinal studies of two individuals (AC13 and PI004) showed that the initial control of viremia was independent of the SL9 CTL response • Low Gag expression levels did not correlate with the delayed CTL response to this epitope • Autologous SL9 variants SLYNTIAVL, SLYNTVAVL, SLFNTVATL, SLFNTVATL, and SLFNTVATL are each capable of inducing a range of CTL responses, sometimes strong, sometimes diminished, and sometimes complete escape relative to the than the wild type variant SLYNTVATL in patients with chronic HIV-1 infection – the ability to cross-react with a particular variant was patient dependent			
p17 (77–85)	p17	SLYNTVATL	HIV-1 infection	human (A*0201)	Altfeld2001c
	• Epitope name: p17 SL9 • HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested • Three additional previously described HLA-A2 epitopes were added to the set of 20, including p17 SL9, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acute infected individuals recognized at least 1 (median of 1 and maximum of 2) • p17 SL9 was recognized in 12/22 patients with chronic HIV-1 infection • Only 1/13 patients with acute HIV-1 infection recognized p17 SL9			
p17 (77–85)	Gag	SLYNTVATL	HIV-1 infection	human (A*0201)	Goepfert2000
	• Epitope name: (SL9) • This paper describes a comparison of results of different CTL assays, a SL9 tetramer assay and IFN-gamma ELISPOT, using 7 HIV-positive patients • The IFN-gamma ELISPOT assay was compared using the single SL9, a pool of overlapping 20 mers, and recombinant vaccinia encoding Gag as antigen – pooled peptides gave the highest number of spot forming cells, vaccinia gave high background • A correlation with results of the tetramer assay was found only for ELISPOT using the Gag epitope as antigen, but the tetramer assay detected a 10-fold higher number of cells than could produce IFN-gamma in the ELISPOT assay – the authors suggest not all tetramer-positive cells may produce IFN-gamma, some may be undergoing apoptosis, some may be producing other cytokines • The tetramer assay could detect a reaction to SLYNTVATL in most of the HLA-A*0201 chronically HIV-1 infected study subjects			

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17 (77–85)	Gag (LAI)	SLYNTVATL	in vitro stimulation	human (A*0201)	Engelmayer2001
	• Recombinant canarypox virus vector containing HIV-1 sequences, upon infection of mature dendritic cells, can trigger specific lysis through in vitro by T-cells from HIV-1 infected individuals at levels comparable to the response seen to HIV carried in vaccinia vectors • Recombinant canarypox virus vector containing HIV-1 sequences can also stimulate HIV-specific CD4+ helper T-cell responses				
p17 (77–85)	p17 (77–85 LAI)	SLYNTVATL	HIV-1 infection	human (A*0201)	Mollet2000
	• Epitope name: G3 • A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using tetramer staining or CD8+ cell IFNgamma production to measure responses • In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished • Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change				
p17 (77–85)	Gag	SLYNTVATL	HIV-1 infection	human (A*0201)	Gea-Banacloche2000
	• In a study including many long-term non-progressors, no correlation between plasma virus levels and number of HIV-specific CD8+ T-cells was found • High frequencies of circulating CD8+ T-cells were HIV-1 specific, and the majority of these responses were to gag-pol gene products • 4/21 subjects were HLA-(A*0201), and of these only 2 subjects (patient 3 and 19) tested positive to this epitope				
p17 (77–85)	p17 (77–85 SF2)	SLYNTVATL	HIV-1 infection	human (A*0201)	Propato2001
	• Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus • Tetramer staining with A2, beta2microglobulin, and either SLYNTVATL, KLVGKLNWA, or LTFGWCFKL revealed that tetramers detected more HIV-specific sells in LTNP than in progressors, activated effector cells were the minority population, and ELISPOT correlated better with the effector cell subpopulation than the total tetramer stained population				
p17 (77–85)	Gag (77–85)	SLYNTVATL	HIV-1 infection	human (A*0201)	Jin2000a
	• The CTL effector levels (CTLe) were compared in long term non-progressors (LTNP) with low viral load and in patients whose virus was well-suppressed by therapy, using a tetramer assay • LTNPs have high memory CTLe numbers and low viral load, while HAART patients had low CTLe numbers and low viral load				
p17 (77–85)	p17 (77–85)	SLYNTVATL	HIV-1 infection	human (A*0201)	Appay2000
	• Combined tetramer and intracellular cytokine staining was used to study the function of circulating CD8+ T cells specific for HIV and CMV • HIV-specific CD8+ T cells expressed lower levels of perforin than CMV-specific CD8+ T cells from the same donor, and this was associated with persistent CD27 expression on HIV-specific cells, suggesting impaired maturation • In most donors, between 50% and 95% of the activated virus-specific CD8+ T cells produced IFN-γ and MIP-1β with a distinct subset that failed to produce TNF-α				
p17 (77–85)	p17 (77–85)	SLYNTVATL	HIV-1 infection	human (A*0201)	Goulder2000b
	• Tetramer assays were compared with three functional assays in 42 people with chronic HIV infection: ELISPOT, intracellular cytokine staining, and precursor frequency (limiting dilution assay [LDA])				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• HIV-specific tetramer staining CTLs appeared to be active, and inert CTL were not found to play a significant role in chronic pediatric or adult HIV infection				
p17 (77–85)	p17	SLYNTVATL	HIV-1 infection	human (A*0201)	Ostrowski2000
	• The role of CD4+ T-cell help in expansion of virus-specific memory CTL was studied through co-culture *ex vivo* • Optimal expansion of HIV-1-specific memory CTL depended on CD4+ T cell help in 9 of 10 patients – CD40 ligand trimer (CD40LT) could enhance CTL in the absence of CD4+ T cell help to a variable degree in most of patients • Those CTL that didn't respond to CD40LT could expand with IL2 present, and IL15 produced by dendritic cells also contributes • The T-helper epitope used for CD4+ T cell stimulation was the universal tetanus helper epitope TET830-843 (QYIKANSKFIGITE)				
p17 (77–85)		SLYNTVATL	Vaccine	human (A*0201)	Ferrari2001
	Vaccine *Vector/Type:* canarypox prime with rgp120 boost, canarypox prime with rgp160 boost *Strain:* gp41 LAI, Gag LAI, gp120 MN, gp120 SF2 *HIV component:* gp120, gp41, Gag, Pol and Nef epitope rich regions • Two vaccinees with Gag responses were HLA-A*0201+, but neither made SLYNTVATL responses to the Gag vaccine, in contrast to its frequent recognition in natural infections. No HLA-A*0201 responses were observed to an Env vaccine.				
p17 (77–85)		SLYNTVATL	HIV-1 infection	human (A*0201)	Migueles2001
	• CTL activity was monitored in 27 individuals, including 10 LTNP with an over-expression of HLA B*5701 – these individuals have viral loads below the threshold of infection without therapy, and their immune response tends to be focused on peptides that contain B*5701 epitopes ISPRTLNAW, KAFSPEVIPMF, TSTLQEQIGW, and QASQEVKNW. • CTL responses are broader in B*5701+ individuals with progressive viremia than those that control viremia. • The HLA-A*0201 SLYNTVATL epitope response was not as strong individuals that carried both A2 and B57.				
p17 (77–85)	Gag (77–85)	SLYNTVATL	HIV-1 infection	human (A*0201)	Sewell2002
	• Epitope processing of three different HLA-A*0201 HIV epitopes was shown to use different pathways, which might influence patterns of immunodominance. .174 cells were used that lack TAP1 and TAP2 genes, as well as the LMP2 and LMP7 genes that encode the beta-subunits of the immunoproteasome. These genes could be added back through transfection to study processing. • ILKEPVHGV was efficiently presented in TAP-1 and -2 transfected cells while VIYQYMDDL and SLYNTVATL were not. VIYQYMDDL was destroyed by the MB1 subunit of the protease, and could be expressed in the presence of the proteasome inhibitor lactacystin, but SLYNTVATL expression was not restored. SLYNTVATL expression was unaltered by lactacystin in a wild type cell line.				
p17 (77–85)	Gag (ADA)	SLYNTVATL	HIV-1 infected monocyte-derived	murine (A*0201)	Poluektova2002
	• Epitope name: SL-9 • Nonobese diabetic NOD-C.B-17 SCID mice were reconstituted with HLA-A*0201 positive human PBL and injected with HIV-1 infected monocyte-derived macrophages MDM in the basal ganglia to provide a mouse model of HIV-1 encephalitis. • HLA-A*0201 CTL responses were detected by tetramer staining in the spleen in seven days, increased through day 14, and the numbers of productively infected were reduced >85% in the second week.				
p17 (77–85)	p17 (77–85)	SLYNTVATL	computer prediction	(A*0201)	Schönbach2002
	• Computational methods (artificial neural networks (ANN), hidden Markov models (HMM), binding matrices based on HLA association rates BIMAS) were used to identify HLA-A*0201 and HLA-B*3501 HIV T-cell epitope candidates from 533 Gag, Env and Pol sequences of which 374 were derived from HIV-1, 97 were derived from HIV-2 and 62 from SIV. Comparisons to known epitopes and between clades were made.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The SLYNTVATL epitope received focused discussion. SLYNTVATL, slFntvatl, slyntvaVl, and slyntIaVl are all recognized variants, ANN predicts all four variants would be recognized, while BIMAS only predicts SLYNTVATL and slFntvatl would be recognized. However, [Sewell1997] suggested certain substitutions may be antagonistic, including slFntvatl, and vaccines do not stimulate SLYNTVATL responses as well as natural infections. The authors note these kinds of issues complicate the application of computational predictions of epitopes to vaccine design.				
p17 (77–85)	Gag (76–84)	SLYNTVATL	Vaccine	murine (A*0201)	Singh2002, Sykes1999
	Vaccine *Vector/Type:* DNA *HIV component:* HIV-1 divided into a 32 plasmids in a ubiquitin expression library • C3H (H-2k) transgenic mice carrying a fused HLA-A*0201 alpha1 and alpha2 and H-2Dk alpha3 hybrid class I molecule were immunized using an epidermal gene gun with an ubiquitin expression library of 32 plasmids that spanned the HIV-1 genome. Ubiquitin targets the expressed HIV-1 peptides to the proteasome. • A single immunization with the UB-HIV-1 library vaccine induced potent, stable and multivalent CTL responses against all library members. • Immunodominant epitopes SLYNTVATL (Gag), ILKEPVHGV(Pol), RIQRGPGRAFVTIGK(P18) and AFHHVAREK (Nef) elicited strong CD8+/IFN- responses and stimulated CTL that were functional in a Cr-release assay and against wild type antigen. • The presence of multiple plasmids HLA-A*0201-restricted CTL epitopes did not decrease CTL immunogenicity, and CTL responses to single peptide immunizations were comparable to responses based on mixtures of either 16 or 32 peptides.				
p17 (77–85)		SLYNTVATL	HIV-1 infection	human (A*0201)	Imami2002b
	• 70 patients with chronic disease progression, 10 clinical non-progressors, and 3 immunologically discordant progressors (individuals who controlled viremia but had progressive CD4+ T-cell decline) were analyzed for their T-helper cell responses to p24 and cytokine profile. Long term non-progressors had much strong Th responses, particularly to p24 peptides, and they tended to be balanced between Th1, IL-2 producing and Th2, IL-4 producing responses. • One of the immunologically discordant progressors became symptomatic during the course of the study, and he had a rapid drop in proliferative response to all antigens and also a shift from a Th1 to a Th2 response. To find out if the CD8 response also shifted in cytokine production, the CD8+ T-cell response to SLYNTVATL in this patient was also tested. It to was found to shift, from IFNgamma to IL-4 producing in Elispot, and using a bioassay of indicator lines, from IL-2 to IL-4 production.				
p17 (77–85)	p17 (77–85)	SLYNTVATL		human (A*0202)	Brander2001
	• C. Brander notes that this epitope can be presented by A*0201 and A*0202				
p17 (77–85)	p17 (SF2)	SLYNTVATL	HIV-1 infection	human (A*0202)	Goulder2000a
	• The CTL-dominant response was focused on this epitope in 11/25 HLA A2 (A*0201 or A*0202) HIV+ individuals from Boston and in 1/8 HLA A2 HIV+ individuals from Durban • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK(p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa				
p17 (77–85)	p17 (77–85 LAI)	SLYNTVATL		human (A*0205)	Brander2001
	• C. Brander notes that this epitope can be presented by A*0201 and A*0202				
p17 (77–85)	p17 (subtype A)	SLYNTVATL	HIV-1 exposed seronegative	human (A*0214, A*0201)	Kaul2000
	• 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 gamma-IFN responses in the cervix – systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Low risk individuals did not have such CD8+ cells • CD8+ T cell epitopes: DTVLEDINL (3 individuals), SLYNVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women • The epitope variants SLYNTVATL and SLFNTVATL were both recognized				
p17 (77–85)		SLYNTVATL	HIV-1 infection	human (A02)	Sabbaj2002b
	• Epitope name: Gag-SL9 • Among HIV+ individuals who carried HLA A02, 17/30 (57%) recognized this epitope				
p17 (77–85)	Gag (77–85) **Vaccine** *Vector/Type:* vaccinia *HIV component:* polyepitope	SLYNTVATL	Vaccine	human (A2)	Woodberry1999
	• A polyepitope vaccine was generated in a vaccinia construct that contiguously encoded seven epitopes, all presented by HLA A-2 • HHD mice have a transgene of HLA A2 linked to the transmembrane and cytotoxic domains of H-2D^d – this transgene is the only MHC molecule expressed in the mice • CTL responses to Gag (77-85) SLYNTVATL, Pol (476-484) ILKEPVHGV, gp120 (120-128) KLTPLCVTL, and Nef (190-198) AFHHVAREL were observed in HIV polytope HHD-vaccinated mice, and these responses were enhanced with vaccinia boost • No CTL immune responses were generated against HLA A2-restricted HIV epitopes Nef 157-166 (PLTFGWCYKL), Pol 346-354 (VIYQYMDDL), and Nef 180-189 (VLEWRFDSRL) • Sixteen HLA A2+ patients were tested for their ability to make CTL responses by peptide restimulation in culture with the epitopes selected for inclusion in the polytope – one individual recognized all seven of these epitopes; 7 patients had CTL cultures able to recognize at least one of the epitopes, and 6 of those 7 recognized more than one epitope, but they were not able to test all peptides for all patients; many patients only had three peptides tested • SLYNTVATL was recognized by 5/16 HLA-A2 patients			
p17 (77–85)	p17 (77–85) **Vaccine** *Vector/Type:* canarypox *Strain:* MN, LAI *HIV component:* gp120, gp41, Gag, Protease	SLYNTVATL	Vaccine	human (A2)	Carruth1999
	• The vaccine used was a live recombinant canarypox (CP) virus vaccine containing multiple HIV-1 genes (HIV-1 MN gp120, HIV-1 LAI gp41, HIV-1 LAI Gag, HIV-1 LAI protease) • CD4+ and CD8+ Gag and Env specific CTL responses were detected in only 1/5 vaccinated volunteers, and were not detectable 1 year after vaccination • CTL responses to epitopes SLYNTVATL and TVYYGVPVWK from HIV+ control patients were used as positive controls • The study explored why vaccinees were non-responsive – non-response was not due to inherent defects or differences in the ability of these individuals to process and present antigen • Lack of response to SLYNTVATL led the authors to speculate that the immunodominance of this epitope in natural infections may not be recapitulated by vaccine antigen				
p17 (77–85)	p17 (77–85) • Epitope name: SL9 • A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs	SLYNTVATL	HIV-1 infection	human (A2)	Birk1998b
p17 (77–85)	p17 (77–85) • Epitope name: SL9 • Included as a negative control in a tetramer study of A2-EBV CTL response	SLYNTVATL	HIV-1 infection	human (A2)	Callan1998
p17 (77–85)	p17 • Epitope name: SL9	SLYNTVATL	HIV-1 infection	human (A2)	Wagner1998a

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• CTL specific for HIV epitopes were used to show that the mediators of both the cytolytic (granzyme A was used as the marker) and non-cytolytic (HIV-1 inhibitory chemokines MIP-1 α and RANTES were used as markers) anti-viral responses are localized within the CTL's cytotoxic granules				
p17 (77–85)	p17 (77–85 HXB2) • Epitope name: SL9 • Two CTL clones recognize this epitope, but not the NL4-3 form of the epitope SLYNTIAVL • Nef down-regulates MHC class I molecules, which inhibits CTL killing, and this down-regulation can be partially compensated for by adding excess soluble peptide	SLYNTVATL	HIV-1 infection	human (A2)	Collins1998
p17 (77–85)	p17 (77–85) • Epitope name: SL9 • Cross-clade CTL response was studied by determining the CTL activity in seven patients from Bangui, (6 A subtype, and 1 AG recombinant infections) and one A subtype infection from a person living in France originally from Togo, to different antigens expressed in vaccinia • Pol reactivity: 8/8 had CTL to A subtype, and 7/8 to B subtype, and HIV-2 Pol was not tested • Gag reactivity: 7/8 reacted with A or B subtype gag, 3/8 with HIV-2 Gag • Nef reactivity: 7/8 reacted with A subtype, and 5/8 with B subtype, none with HIV-2 Nef • Env reactivity: 3/8 reacted with A subtype, 1/8 with B subtype, none with HIV-2 Env • Patient B18 had the greatest breadth and diversity of response, and recognized Gag SLYNTVATL and Nef PLTFGWCFKL	SLYNTVATL	HIV-1 infection	human (A2)	Durali1998
p17 (77–85)	p17 (77–85) • Epitope name: SL9 • Allogeneic dendritic cells (DCs) were obtained from HLA-identical siblings, pulsed with rgp160 MN or A2-restricted HIV-1 epitope peptides, and infused monthly into six HIV-infected patients • 1/6 showed increased env-specific CTL and increased lymphoproliferative responses, 2/6 showed increase only in proliferative responses, and 3/6 showed no change – pulsed DCs were well tolerated • SLYNTVATL is a conserved HLA-A2 epitope included in this study – 3/6 patients had this sequence as their HIV direct sequence, one had the form SLYNTVAVL and all four of these had a detectable CTL response – the other two had either the sequence SLFSAVAVL or SLFSAVAAL and no detectable CTL response	SLYNTVATL	HIV-1 infection	human (A2)	Kundu1998b
p17 (77–85)	p17 (77–85 IIIB) • Epitope name: SL9 • HIV IIIB proteins were used to define the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB • SLYNTVAVL, a variant found in HIV-1 MANC, was also recognized • SLFNTVAVL, a variant found in HIV-1 NY5CG, was also recognized	SLYNTVATL	HIV-1 infection	human (A2)	Sipsas1997
p17 (77–85)	p17 • Epitope name: SL9 • A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating • The A subtype consensus is SLfNtvatL • The D subtype consensus is SLyNTvATL	SLYNTVATL	HIV-1 infection	human (A2)	Rowland-Jones1998a
p17 (77–85)	p17 • Epitope name: SL9 • Naturally occurring variants of this epitope escaped killing and acted as antagonists	SLYNTVATL	HIV-1 infection	human (A2)	Sewell1997

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The following variants were found in HIV-1 infected patients who mounted a strong response against this epitope: –F——, –F—-V-, –S——, -SF——, –L——, ——I—, ——I-V-, –F–I—, –F–I-V-, –F-A—- • All variants bound to A2 with at least half the affinity of SLYNTVATL except the triple mutant: –F–I-V- • Antagonism could be observed at low concentrations, abrogating lysis at an antagonist:agonist ratio of 1:10 – the antagonism was observed in one SLYNTVATL-specific CTL line but not another				
p17 (77–85)	p17 (77–85 HXB2) • Epitope name: SL9 • A chimeric universal T cell receptor was created by linking CD4 or an HIV-specific anti-gp41 Ig sequence to the signaling domain of the T cell receptor chain ζ, and transduced into CD8+ cells • The response using universal-receptor-bearing CD8+ cells to lyse infected cells in vitro was comparable to the natural occurring responses of CTL-clones from HIV+ individuals in terms of kinetics and efficiency • A CTL clone specific for this epitope was used for the comparison	SLYNTVATL	HIV-1 infection	human (A2)	Yang1997b
p17 (77–85)	p17 (77–85) • Epitope name: SL9 • Keyhole limpit hemocyanin or tetanus toxoid Th epitope co-expression with peptide CTL epitopes on the same APC was required for induction of peptide-specific CTL	SLYNTVATL	in vitro stimulation	human (A2)	Stuhler1997
p17 (77–85)	p17 (77–85) • Epitope name: SL9 • CD4+ cell lines acutely infected with HIV were studied to determine their susceptibility to lysis by CTL • Clones specific for RT lysed HIV-1 infected cells at lower levels than Env or Gag specific clones • The distinction was thought to be due to lower expression of RT relative to Env and Gag • CTL can lyse infected cells early after infection, possibly prior to viral production	SLYNTVATL	HIV-1 infection	human (A2)	Yang1996
p17 (77–85)	p17 (77–85) • Epitope name: SL9 • CTL inhibit HIV-1 replication at effector cell concentrations comparable to those found in vivo • CTL produced HIV-1-suppressive soluble factors – MIP-1α, MIP-1β, RANTES, after antigen-specific activation • CTL suppress HIV replication more efficiently in HLA-matched cells	SLYNTVATL	HIV-1 infection	human (A2)	Yang1997a
p17 (77–85)	p17 (77–85 LAI) • Epitope name: SL9 • Examined in the context of motifs important for HLA-A2 binding	SLYNTVATL	HIV-1 infection	human (A2)	Parker1992, Parker1994
p17 (77–85)	p17 (77–85 LAI) • Epitope name: SL9 • Review of HIV CTL epitopes	SLYNTVATL	HIV-1 infection	human (A2)	McMichael1994
p17 (77–85)	p17 (77–85) • Epitope name: SL9 • CTL clones recognize naturally processed peptide	SLYNTVATL	HIV-1 infection	human (A2)	Tsomides1994
p17 (77–85)	p17 (77–85) • Epitope name: SL9	SLYNTVATL	in vitro stimulation	human (A2)	Stuhler1997

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• A three cell-type cluster consisting of APCs, Th, and CTLs is the minimal regulatory unit required for Th cell-dependent induction of CTLs				
p17 (77–85)	p17 (77–85) • Epitope name: SL9 • The consensus peptides of B and D clade viruses and some Cs have the sequence SLYNTVATL • The consensus peptide of A, and some C strains have SLFNTVATL, a form that is cross-reactive	SLYNTVATL	HIV-1 infection	human (A2)	Cao1997a
p17 (77–85)	Gag (77–85) • Epitope name: SL9 • CTL specific responses were measured over a 1.3 to 1.5 year period in members of the Sydney Blood Bank Cohort (SBBC) who had been infected with a natural attenuated strain of HIV-1 which was Nef-defective • Some of these patients had prolonged high levels of CTL effector and memory cells despite low viral load	SLYNTVATL	HIV-1 infection	human (A2)	Dyer1999
p17 (77–85)	p17 (77–85) • Epitope name: SL9 • Two overlapping epitopes were recognized in a long-term survivor, restricted by two different HLA molecules, HLA-A11(TLYCVHQR) and -A2 (SLYNTVATL) • Viral sequence substitutions were present in this individual which did not affect viral replication and did not alter CTL-recognition of the A2 epitope, but reduced recognition of the A11 epitope, indicative of immune escape	SLYNTVATL	HIV-1 infection	human (A2)	Harrer1998
p17 (77–85)	p17 (77–85 SF2) • The relative contribution of CTL responses against HIV-1 Vpr, Vpu, and Vif were analyzed in multiple HIV-1-infected individuals • Individuals with long-term nonprogressive and treated chronic HIV-1 infection targeted Vpr more frequently than individuals with treated acute infection • Vpr is a frequent target of HIV-1 specific CD8+ T-cells – a response was detected in 45% of individuals tested and Vpr and p17 were the most preferentially targeted proteins per unit length by CD8+ T-cells • The A2 eptiopes Vpr AIIRLLQQL and p17 SLYNTVATL do not account for the dominance of Vpr and p17, the result holds even when HLA-A2+ individuals are excluded	SLYNTVATL	HIV-1 infection	human (A2)	Altfeld2001a
p17 (77–85)	p17 (BRU) • Epitope name: SL9 • Exogenous presentation or cross-presentation of epitopes by antigen presenting cells (APC) without protein synthesis is an alternative pathway for CTL epitope processing that may be important in the initial generation of viral specific CTL • Dendritic cells treated with AZT to inhibit protein synthesis were able to elicit a strong specific CTL response in SLYNTVATL specific CTL line EM71-1 without protein synthesis, while macrophages demonstrated a decreased presentation efficiency • Exogenous Gag epitope presentation was Env-dependent and required receptor-dependent fusion	SLYNTVATL	in vitro stimulation	human (A2)	Buseyne2001
p17 (77–85)	p17 • HLA tetramers to six epitopes were used to study HLA-A2, B8 and B57 CTL in 54 patients – HIV-specific tetramer positive cells were inversely correlated with viral load in patients with high CD4, but in patients with CD4 T-cells below 400 high tetramer frequencies were found despite high viral load • Most patients have high levels of HIV-specific T-cell expansions, but many of these cells aren't functional • In 15 of the patients, the proportion of IFN gamma producing tetramer cells correlated with AIDS-free survival • In one patient with a SLYNVATL response, no SLYNVATL mutations were found among 21 clones despite high viral load (260,000 RNA copies/ml serum), suggesting low in vivo efficacy of the SLYNVATL response	SLYNVATL	HIV-1 infection	human (A2)	Kostense2001

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17 (77–85)	p17 (77–85)	SLYNTVATL	HIV-1 infection	human (A2)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
p17 (77–85)	p17	SLYNVATL	HIV-1 infection	human (A2)	Seth2001
	• CTL responses were studied by tetramer staining in 41 patients with combination therapy – activated CD8+ T-cells decline as the viral load drops in response to therapy, but the overall level of antigen-specific cells capable of differentiating into effectors stays constant and new epitopes may be recognized • 6/10 A*0201+ individuals had HIV-specific tetramer staining cells, and 5 of these declined upon successful therapy • 4/10 A*0201+ individuals with chronic HIV-1 infection recognized this epitope • Prior to therapy, the mean percentage of CD8+ cells that recognized the immunodominant epitope SLYNVATL was six-fold greater than the percentage recognizing the epitope ILKEPVHGV				
p17 (77–85)	p17 (77–85)	SLYNTVATL	HIV-1 infection	human (A2)	Islam2001
	• Epitope name: SL9 • Transcript frequencies were followed for four CTL clones from patient 115, with a chronic and stable HIV-1 infection, were tracked in a longitudinal study of samples collected 6-11 years post infection: clone M21 and E15 recognize ERYLKDQQL,and clone D87 recognizes variant ERYLQDQQL, and clone p175b recognizes the A2 epitope SLYNTVATL • This epitope sequence from clone p175b uses the Vbeta5, CDR3 (FDS), Jbeta2.7 TCR beta gene • Responses were stable even through HAART with undetectable viral loads, but frequencies varied over time by 100-fold, ranging from 0.012% of the total population for SLYNTVATL at its lowest point to 3.78% for M21, with the relative frequencies of clones shifting over time				
p17 (77–85)	p17 (77–85 SF2)	SLYNTVATL	HIV-1 infection	human (A2)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-A2+ individuals that had a CTL response to this epitope broken down by group: 1/10 group 1, 2/6 group 2, and 2/4 group 3				
p17 (77–85)	p17 (77–85)	SLFNTVATL	HIV-1 infection, HIV-1 exposed seronegative	human (A2)	Kaul2001a
	• Variants SL(F/Y)NTVATL are A/B clade specific • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure • Among HLA-A2 women, 1/10 HEPS and 22/26 HIV-1 infected women recognized this epitope, likelihood ratio 18.3, p value < 0.003, and ILK(D/E)PVHGV tended to be more reactive in HEPS women, SL(F/Y)NTVATL in infected women • The dominant response to this HLA allele was to this epitope in the 1/10 HEPS case and in 18 of the 22/26 HIV-1 infected women that responded • Differences in epitope specificity were only seen for responses restricted by class I HLA alleles A2, A24, A*6802, B14, and B18, previously shown to be associated with resistance to HIV-1 in this cohort				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Subject ML 1250 had an A2 response to ILK(D/E)PVHGV prior to seroconversion, which switched to SL(F/Y)NTVATL post-seroconversion • Subjects ML 1575 and ML 1592 had no response to SL(F/Y)NTVATL prior to seroconversion, but made responses post-seroconversion • Subject ML 1760 had an A2 response to ILK(D/E)PVHGV prior to seroconversion, and gained responses to epitopes A2 SL(F/Y)NTVATL and B27 KRWII(L/M)GLNK post-seroconversion				
p17 (77–85)	p17 (77–85 93TH253 subtype CRF01) • Epitope name: G77-85 • This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand • HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed • This epitope was reactive in HIV+ control study subjects 125 and 144 who carried HLA-A2	SLYNTIATL	HIV-1 infection	human (A2)	Sriwanthana2001
p17 (77–85)	p17 (77–85 93TH253 subtype CRF01) • More than half of a cohort of HIV+ female sex workers (FSW) from Northern Thailand were HLA-A11 positive, and this study concentrated on A11 epitopes in this group, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested. • 2/4 tested FSWs recognized the E clade version of this epitope, SLYNTIATL, the B clade version is SLYNTVATL • This epitope was only conserved in CRF01 and subtypes B and D, and exact matches were uncommon	SLYNTIATL	HIV-1 infection	human (A2)	Bond2001
p17 (77–85)	p17 (77–85) • The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person • SLYNTVATL was the dominant A2 epitope recognized in patients with chronic infection, except for Subject 11841 who recognized 5/8 epitopes • Three subjects had an A2 response only to SLYNTVATL • The two subjects with acute infection did not respond to SLYNTVATL	SLYNTVATL	HIV-1 infection	human (A2)	Day2001
p17 (77–85)	p17 (77–85) • Epitope name: SL9 • Immune escape variants in this epitope where transmitted both horizontally and vertically in two families • Eight transmitting mothers and 14 non-transmitters mothers were studied and variation within the SL9 epitope was associated carrying HLA-A2 (P=0.04), but no link between variation from the SL9 consensus and vertical transmission was established	SLYNTVATL	HIV-1 infection	human (A2)	Goulder2001c
p17 (77–85)	p17 (SF2) • This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual • The response to the peptide was CD8 dependent, but the HLA presenting molecule and optimal epitope were not determined	SLYNTVATL	HIV-1 infection	human (A2)	Altfeld2000b
p17 (77–85)	p17 (77–85 LAI) • Ritonavir (RTV) inhibits chymotryptic activity in the 20S proteasome in vitro, as does Saquinavir (SQV) to a lesser extent; Indinavir (IDV) does not. Thus there is concern protease inhibitors may adversely effect CTL epitope processing, but this paper indicates that processing is not inhibited at therapeutically relevant concentrations of RTV when the proteasome is functioning in in an intracellular context.	SLYNTVATL	HIV-1 infection	human (A2)	Kelleher2001a

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• RTV did not reduce antigen presentation and concentration of the two immunodominant Gag CTL epitopes (KRWIIMGLNK (B27) and SLYNTVATL (A2)). • RTV did not inhibit the processing and assembly of HLA-B35 or -A2, which are assembled with a rapid and moderate time course, respectively, or of HLA-A3, -B27 and -B39.				
p17 (77–85)	p17	SLYNTVATL	HIV-1 infection	human (A2)	Kaul2002
	• Neisseria gonorrhea cervititis in 9 HIV+ Kenyan sex workers caused a functional deficiency in IFN-gamma production in HIV-1 epitope-specific CD8+ T-cells, detected by intracellular cytokine production and tetramer assays, while not affecting the total number of epitope-specific CTLs. • Ghonorrhea caused the weaker HIV-1 specific CTL responses in 4 HIV-1 exposed persistently seronegative (HEPS) women to become undetectable by Elispot and tetramer assays, and CMV-specific CTL in 2 HEPS subjects were shown to have impaired function with regard to IFN-gamma production.				
p17 (77–85)	Gag (p17) (77–85 NL43)	SLYNTVATL	HIV-1 infection	human (A2)	Yang2002
	• Nef down-modulates class I protein expression, and this study demonstrates directly that Nef-deleted HIV-1 NL-43 can be more effectively killed in vitro than NL-43 with an intact Nef. The effect was shown to be specific for class I presentation of epitopes, and unlike Nef, deleting Vpr did not alter CTL susceptibility of NL-43. The CTL clone 18030D23, specific for the class I A2 presented SLYNTVATL epitope, was one of four used in this study.				
p17 (77–85)	p17 (77–85 BRU)	SLYNTVATL	HIV-1 infection	human (A2)	Cohen2002
	• The antigen presentation of two A2-restricted epitopes was compared, SLYNTVATL (p17) and ILKEPVHGV (RT). HIV-1 infected cells were more sensitive to lysis by SLYNTVATL-specific CTL than by ILKEPVHGV-specific CTL, because of a higher density of SLYNTVATL-A2 resulting from differences in processing. • Incubation with a T1-cell proteolytic extract showed that by four hours, 25% of a p17 peptide had a C-term Leu-85 and were SLYNTVATL-precursors, while ILKEPVHGV-precursors were far less frequent (6.8%) even with four times more proteolytic extract after 30 hours. • p17 was preferentially cleaved between Leu85 and Tyr86, while appropriate Val484 and Tyr485 cleavage was minor for RT. • In a competition experiment, RSLYNTVATL bound TAP 3.7-fold more efficiently than RT peptides. • No difference in CTL avidity was detected in six patients with HLA-A2-restricted responses to these epitopes. • No significant difference in HLA-A2 binding of to p17 or RT epitopes was observed.				
p17 (77–85)	p17 (77–85)	SLYNTVATL	Vaccine	murine (A2)	Kmieciak2001
	Vaccine *Strain:* IIIB *HIV component:* Gag, Pol *Adjuvant:* IL-12 (IL-12p35 and IL-12p40) • Transgenic mice expressing a HLA-A2/Kb chimeric protein were vaccinated with either a p17-p24-p51 fusion protein (vG/P-92) or the Gag-Pol precursor protein (vVK1). • Compared to vVK1, vG/P-92 induced a significant increase in Gag and Pol induced IFNgamma production and CTL responses, and to the epitopes SLYNTVATL and ILKEPVHGV, as determined by Elispot and 51Cr-release assays.				
p17 (77–85)	Gag (77–85)	SLYNTVATL	HIV-1 infection	human (A2)	Appay2002
	• Four HIV patients with prolonged clinically successful anti-viral therapy but with ongoing evidence of replication and Nef mRNA transcription, showed specific T-cell responses by Elispot and Tetramer staining, maintained for 2-4 years after initiation of HAART. • Nef epitope recognition was detected in all 4 subjects, gp120, Pol and Gag-specific in 1 or 2 subjects. • The HIV-specific CD8+ T-cells had an intermediate maturation phenotype characterized by low levels of perforin and high levels of CD27 expression.				
p17 (77–85)	p17	SLYNTVATL	HIV-1 exposed seronegative	human (A2, A*0202)	Rowland-Jones1998b
	• Epitope name: SL9 • HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes • This epitope is conserved among B and D clade viruses • The Clade A version of the epitope, SLFNTVATL, was preferentially recognized by CTL • This epitope was recognized by two different exposed seronegative prostitutes				
p17 (77–85)	p17 (77–85 LAI)	SLYNTVATL	Vaccine	murine (A2.1)	Peter2001
	Vaccine *Vector/Type:* peptide *Strain:* LAI *Adjuvant:* P30, incomplete Freund's adjuvant (IFA), Montanide (ISA 720), PLG-microparticle • Epitope name: LR23 • The stability of peptide binding to HLA-A2.1 was determined for six HLA-A2.1 peptides included in this vaccine study – ILKEPVHGV (RT), SLYNTVATL (p17), SLLNATDIAV (gp41) and LLWKGEGAV (RT) all bound with high affinity comparable to a influenza epitope reference (GILGFVFTL), while RGPGRAFVTI and VIYQYMDDL bound with a lower affinity (relative binding activity = 0.01). • The four high-affinity peptides formed stable complexes with half-lives ranging between 8 and 32 hours, while the low affinity peptides had half lives of less than an hour. • HLA-A2.1 transgenic mice were immunized with the six HIV-1 peptides and P30, as a universal T-helper epitope, with IFA or Montanide or microspheres as adjuvants. • All peptides except VIYQYMDDL induced a stong CTL response in Cr-release assays - stronger responses were observed when peptides were delivered alone, indicating immunodominance when the combination was used.				
p17 (77–85)	p17 (77–85 LAI)	SLYNTVATL	Vaccine	murine (A2.1)	Peter2002
	Vaccine *Vector/Type:* peptide *Strain:* LAI *Adjuvant:* P30, incomplete Freund's adjuvant (IFA), IL-12 • Epitope name: LR23 • When HIV-1 peptides were used to vaccinate HLA-A2.1 transgenic A2-Kb mice, strong responses to five peptides were observed when the peptides were given individually, but immunodominance limited the response to some of the peptides when they were given in combination [Peter2001]. IL-12 can counteract immunodominance in BALB/c mice, so it was given with the multiple epitope vaccination, and was instead found to specifically eliminate the HLA-A2.1-epitope CTL responses, but not Kb CTL responses. This was possibly a consequence of transient depletion of T-cells, B cells and macropahges in the spleen.				
p17 (77–85)	p17	SLYNTVATL	HIV-1 infection	human (B*0201)	Wilson2000a
	• Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load was also found • All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39 • ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK • The subject with A*0201 had a moderatly strong response to SLYNTVATL • Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705 • No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL			
p17 (77–85)	p17 (77–85)	SLYNTVATL	HIV-1 infection	human (B62)	Goulder1997a
	• Epitope name: SL9				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This paper is a review of CTL and immune evasion, but it presents a study of a shift from an HLA-A*0201 response to SLYNTVATL, to a B62 response to GLNKIVRMY • As long as a strong CTL response to SLYNTVATL was evident, the epitope variants SLFNTVATL or SLYNTIATL dominated the viral population – eventually the CTL response to the index peptide became undetectable, the CTL response shifted to a focus on GLNKIVRMY, and the index peptide SLYNTVATL once again established itself as the dominant form				
p17 (77–85)	Gag (77–85)	SLYNTVATL		human (HLA-A201)	Sandberg2000
	• This epitope served as a positive control in a study comparing peptide binding affinity to HLA-A201 to CTL responses upon vaccination with a nef DNA vaccine				
p17 (82–91)	p17 (82–91 93TH253 subtype CRF01)	IATLWCVHQR	HIV-1 infection, HIV-1 exposed seronegative	human (A11)	Sriwanthana2001
	• Epitope name: G82-91 • This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand • HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed • This epitope was weakly reactive in the HEPS study subject 265 who was HLA A2/A11 • This epitope was strongly reactive in HIV+ study subject 053 who carried HLA-A11				
p17 (82–91)	p17 (82–91 93TH253 subtype CRF01)	IATLWCVHQR	HIV-1 infection	human (A11)	Bond2001
	• HLA-A11 CRF01 (called subtype E in Bond et al.) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive • 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 finding and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified • This epitope was predicted by the EpiMatrix method to be likely to bind to A11, and it served as an epitope in the FSWs, it was one of the six A11 epitopes that had been previously defined • 3/8 tested FSWs recognized this epitope • This epitope was not conserved in other subtypes, and exact matches were uncommon				
p17 (84–91)	Gag (83–90)	TLYCVHQR	HIV-1 infection	human (A*1101)	Fukada2002
	• Counterparts for eight known clade B HLA A*1101 epitopes were generated for clade E (CRF01). Three epitopes, identical among clade A-E, were cross-reactive and recognized by clade E infected individuals. The clade E and B analogs to three more HLA A*1101 epitopes was recognized in a clade specific manner. Two other HLA A*1101 clade B defined epitopes were found not to have stimulated a response in clade E infected individuals. • TLYCVHQR was found to elicit clade-specific responses in clade B (TLYCVHQR is most common, and is also common in clade A – the variant tlycvhqK is common in clade B) and clade E (tlWcvhqr is most common). TLYCVHQR was not recognized by any CTL, tlycvhqK was recognized by CTL from 1/5 B clade infected Japanese subjects, and tlWcvhqr was not recognized by CTL from infected Thai subjects, so this seems to be a B clade exclusive epitope. • The binding of the variant peptides to HLA A*1101 was comparable, but CTL that recognized tlycvhqK did not cross-recognize the other forms, implicating TCR interaction differences.				
p17 (84–91)	p17 (83–91)	TLYCVHQR	HIV-1 infection	human (A11)	Harrer1998
	• Two overlapping epitopes were recognized in a long-term survivor, restricted by two different HLA molecules, HLA-A11(TLYCVHQR) and -A2 (SLYNTVATL)				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Viral sequence substitutions were present in this individual which did not affect viral replication and did not alter CTL-recognition of the A2 epitope, but reduced recognition of the A11 epitope, indicative of immune escape • A Q90E substitution resulted in a loss of the ability of the peptide to induce lysis, a R91K substitution was still reactive, and a R91Q substitution show a reduced ability to stimulate lysis				
p17 (84–92)	p17 (84–92) • C. Brander notes that this is an A*1101 epitope	TLYCVHQRI	HIV-1 infection	human (A*1101)	Brander2001
p17 (84–92)	p17 (84–92) • Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study	TLYCVHQRI	HIV-1 infection	human (A11)	Brander1995b
p17 (84–92)	p17 (84–92) • A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs	TLYCVHQRI	HIV-1 infection	human (A11)	Birk1998b
p17 (84–92)	p17 (84–92) • One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles	TLYCVHQRI	HIV-1 infection	human (A11)	Ferrari2000
p17 (84–92)	p17 (84–92 SF2) • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-A11+ individuals that had a CTL response to this epitope broken down by group: 0/3 group 1, 0/0 group 2, and 1/2 group 3	TLYCVHQRI	HIV-1 infection	human (A11)	Altfeld2001b
p17 (84–92)	p17 (84–92) • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers	TLYCVHQRI	HIV-1 infection, HIV-1 exposed seronegative	human (A11)	Kaul2001a
p17 (86–101)	p17 (SF2) • This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual • The response to the peptide was CD8 dependent, but the HLA presenting molecule and optimal epitope were not determined	YCVHQRIEIKDTKEAL	HIV-1 infection	human	Altfeld2000b
p17 (86–101)	p17 (SF2) • This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual • The response to the peptide was CD8 dependent, but the HLA presenting molecule and optimal epitope were not determined	YCVHQRIEIKDTKEAL	HIV-1 infection	human	Altfeld2000b
p17 (87–105)	p17 (91–105 SF2) • CTL expanded ex vivo were later infused into HIV-1 infected patients	CRIDVKDTKEALEKIE	HIV-1 infection	human	Lieberman1997b

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17 (88–115)	p17 (88–115 ARV)	VHQRIEIKDTKEALDKIEE-EQNKSKKKA	HIV-1 infection	human (A2)	Achour1990
	• B cell epitope HGP-30 also serves as a CTL epitope				
p17 (88–115)	p17 (88–115 ARV)	VHQRIEIKDTKEALDKIEE-EQNKSKKKA	Vaccine	murine BALB/c (H-2^d)	Hamajima1997
	Vaccine *Vector/Type:* peptide *HIV component:* V3, HPG30, CD4BS *Adjuvant:* IL-12 • B cell epitope HGP-30 also serves as a CTL epitope • Vaccine combined HGP-30, V3 loop peptide variants, and CD4 binding site peptide • IL-12 expression plasmid included with the vaccination enhanced the CTL response				
p17 (91–101)	p17 (SF2)	RIDVKDTKEAL	HIV-1 infection	human	Goulder2000a
	• The CTL-dominant response was focused on this epitope in an HIV+ Haitian living in Boston, who was A23/68 B45/72 Cw2/16 – this epitope fell outside the most recognized peptides in the study • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK(p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa			
p17 (91–105)	p17 (91–105 SF2)	RIDVKDTKEALEKIE	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag • One of these 12 had CTL response to this peptide • The responding subject was HLA-A3, A24, B8, B55				
p17 (92–101)	p17 (92–101)	IEIKDTKEAL	HIV-1 infection	human (B*4001)	Brander2001
	• C. Brander notes this is a B*4001 epitope				
p17 (92–101)	p17	IEIKDTKEAL	HIV-1 infection	human (B60)	Wagner1998a
	• CTL specific for HIV epitopes were used to show that the mediators of both the cytolytic (granzyme A was used as the marker) and non-cytolytic (HIV-1 inhibitory chemokines MIP-1 α and RANTES were used as markers) anti-viral responses are localized within the CTL's cytotoxic granules				
p17 (92–101)	p17 (92–101 SF2)	IEIKDTKEAL	HIV-1 infection	human (B60)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-B60+ individuals that had a CTL response to this epitope broken down by group: 0/2 group 1, 1/1 group 2, and 0/0 group 3			

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17 (92–101)	Gag (92–101)	IEIKDTKEAL	HIV-1 infection	human (B60)	Yang2002
	• Nef down-modulates class I protein expression, and this study demonstrates directly that Nef-deleted HIV-1 NL-43 can be more effectively killed in vitro than NL-43 with an intact Nef. The effect was shown to be specific for class I presentation of epitopes, and unlike Nef, deleting Vpr did not alter CTL susceptibility of NL43 infected cells. The CTL clone 161JD27, specific for the class I B60 presented epitope IEIKDTKEAL, was one of four used in this study.				
p17 (92–101)	p17 (SF2)	IEIKDTKEAL	HIV-1 infection	human (B60(B*4001)	Altfeld2000b
	• This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes • B60 is present in 10-20% of the Caucasoid and very common in Asian populations				
p17 (92–101)	p17 (92–101)	IEIKDTKEAL	HIV-1 infection	human (B60/B61)	Day2001
	• No immunodominant responses were detected to five B61-restricted epitopes tested • All five B60-restricted epitopes were reactive in another subject, and the B60-restricted responses together contributed over one-third of the total CTL response				
p17 (93–101)	p17 (SF2)	DVKDTKEAL	HIV-1 infection	human	Goulder2000a
	• The CTL-dominant response was focused on this epitope in a HIV+ Caucasian from Boston, who was A1/*0201 B8/63 Cw7/- – this epitope fell outside the most recognized peptides in the study • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK(p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa				
p17 (93–101)	p17 (93–101)	EIKDTKEAL	Peptide-HLA interaction	human (B8)	DiBrino1994b
	• Examined in the context of motifs important for HLA-B8 binding, predicted epitope based on Achour et al.				
p17 (93–101)	p17 (93–101)	EIKDTKEAL	HIV-1 infection	human (B8)	Birk1998b
	• A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs				
p17 (93–101)	p17 (93–101 LAI)	EIKDTKEAL		human (B8, B60)	Brander1997
	• Pers. Comm. from A. Trocha and S. Kalams to C. Brander and B. Walker				
p17 (121–132)	p17 (121–132 HXB2R)	DTGHSNQVSQNY	HIV-1 infection	human (A33)	Buseyne1993b
	• Clustering of Gag p24 CTL epitopes recognized in 29 HIV-infected people				
p17 (121–132)	Gag (121–132 LAI)	DTGHSNQVSQNY	HIV-1 infection	human (A33)	Buseyne1993a
	• Vertical transmission of HIV ranges from 13% to 39% • Primary assays showed cytotoxic activity against at least one HIV protein was detected in 70% of infected children • Epitopes recognized in five children were mapped using synthetic peptides and secondary cultures • Patient EM17 (CDC P2A+C+D2) had a CTL response to two epitopes in Gag				
p17 (124–132)	p17 (124–132 LAI)	NSSKVSQNY	HIV-1 or HIV-2 infection	human (B*3501)	Brander2001
	• Noted by Brander to be B*3501 epitope				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17 (124–132)	p17	NSSQVSQNY	HIV-1 infection	human (B*3501)	Dorrell2001
• The crystal structure of this epitope bound to HLA-B*3501 shows that a serine can fit into the B pocket, which is shared between B35 and B53, with the hydroxyl group of the P2 serine occupying a position almost identical to the P2 proline that was previously considered the anchor motif • Novel B53 epitopes (DTINEEAAEW and QATQEVKNM) were defined in this study that showed that A and T can also serve as P2 anchor residues for the B pocket of HLA-B35 and B53 – while S, T, and P could all fit into the B pocket and form a hydrogen bond, A would not form a bond, so the authors propose compensatory interactions account for the high affinity of QATQEVKNM for B53				
p17 (124–132)	p17 (124–132 LAI)	NSSKVSQNY	HIV-1 infection	human (B35)	McMichael1994
• Review of HIV CTL epitopes					
p17 (124–132)		NSSKVSQNY	HIV-1 infection	human (B35)	Wilson2000a
• Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load was also found • All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39 • ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK • The subject with A*0201 had a moderatly strong response to SLYNTVATL • Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705 • No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL				
p17 (124–132)	p17 (124–132)	NSSKVSQNY	HIV-1 infection	human (B35)	Birk1998b
• A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs					
p17 (124–132)	p17 (124–132 LAI)	NSSKVSQNY	HIV-1 or HIV-2 infection	human (B35)	Rowland-Jones1995b
• Established by titration					
p17 (124–132)	p17 (124–132 LAI)	NSSKVSQNY	in vitro stimulation	human (B35)	Lalvani1997
• A peptide-based protocol was optimized for restimulation of CTLp using optimized peptide and IL-7 concentrations – importantly this protocol does not stimulate a primary response, only secondary – peptide-specific CTLp counts could be obtained via staining with peptide-Class I tetramers • This peptide was one of the B35 presented test peptides used in control experiments showing that the assay gave no activity using lymphocytes from 21 healthy B35 seronegative donors					
p17 (124–132)	p17	NSSKVSQNY		human (B35)	Rowland-Jones1999
• CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5 • In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive • HIV-2 version of this epitope is not conserved: PPSGKGGNY, but the CTLs are cross-reactive – this is one of five B35 CTL epitopes that are cross-reactive, see also [Rowland-Jones1995b]					

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17 (124–132)	p17	NSSKVSQNY	HIV-1 infection	human (B35)	Seth2001
	• CTL responses were studied by tetramer staining in 41 patients with combination therapy – activated CD8+ T-cells decline as the viral load drops in response to therapy, but the overall level of antigen-specific cells capable of differentiating into effectors stays constant and new epitopes may be recognized				
p17 (124–132)	p17 (124–132 SF2)	NSSKVSQNY	HIV-1 infection	human (B35)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-B35+ individuals that had a CTL response to this epitope broken down by group: 0/2 group 1, 0/2 group 2, and 1/1 group 3				
p17 (124–132)		NSSKVSQNY	HIV-1 infection	human (B35)	Sabbaj2002b
	• Epitope name: Gag-NY9 • Among HIV+ individuals who carried HLA B35, 1/21 (5%) recognized this epitope				

II-B-2 p17-p24 CTL Epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17-p24 (127–3)	p17-p24 (127–135 subtype D) • Epitope starts in p17 and ends in p24 • Predicted on binding motif, no truncations analyzed	QVSQNYPIV		human (A*6802)	Dong1998a
p17-p24 (131–6)	p17-p24 (132–140 SF2) • The epitope starts in p17 and ends in p24 • Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402 • This peptide induced CTL in 1/4 HIV-1+ people tested • NYPIVQNL bound to A*2402 with medium strength, and the epitope can be processed in a vaccinia construct and presented – no CTL clone was obtained	NYPIVQNL	HIV-1 infection	human (A*2402)	Ikeda-Moore1997

II-B-3 p24 CTL Epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (8–17)	p24 (140–149)	GQMVHQAISP	HIV-1 infection	human (B57)	Betts2000
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes • 1/11 of the A2+ individuals was HLA A*0201, A1, B57 and responded to four B57 epitopes and two others				
p24 (8–20)	p24 (140–152 IIIB)	GQMVHQAISPRTL	HIV-1 infection	human (Cw3)	Littaua1991
	• Fine specificity of human Cw3 restricted Gag CTL epitope				
p24 (8–27)	p24 (140–159)	GQMVHQAISPRTLNAWVKVV	HIV-1 infection	human (B14)	Musey1997
	• CTL specific for this epitope were found in the peripheral blood but not in the cervical mucosa of one donor				
p24 (9–18)	Gag (173–182)	QMVHQAISPR	HIV-1 infection	human (A3 supertype)	Propato2001
	• Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus • This epitope can bind 3/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801)				
p24 (10–18)	Gag (174–182)	MVHQAISPR	HIV-1 infection	human (A3 supertype)	Propato2001
	• Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus • This epitope can bind 5/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801)				
p24 (11–24)	p24 (SF2)	VQHAISPRTLNAWV	HIV-1 infection	human	Goulder2000a
	• The CTL-dominant response was focused on this epitope in an HIV+ Haitian living in Boston, who was A34/68 B57/71 Cw3/7 – this epitope fell outside the most recognized peptides in the study • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK(p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa				
p24 (11–32)	p24 (143–164 BH10)	VHQAISPRTLNAWVKVVEE-KAF	HIV-1 infection	human (Bw57)	Johnson1991
	• Gag CTL response studied in three individuals				
p24 (12–20)	Gag (146–154)	HQAISPRTL	HIV-1 infection	chimpanzee (Patr-B*02)	Balla-Jhagjhoorsingh1999b
	• Certain HLA-alleles have been associated with long-term survival – among them are HLA-B*27 and HLA-B*57				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Of more than 150 chimpanzees that have been reported to be infected with HIV-1, only one has developed AIDS • CTL responses were studied in two HIV-1 infected chimpanzees that have strong CTL responses, and they were found to respond to highly conserved epitopes that are recognized in humans in the context of HLA-B*27 and HLA-B*57 • The human HLA protein which presents this Patr-B*02 epitope is HLA-B*5701 but the amino acid sequences in the binding pockets of HLA-B*5701 and Patr-B*02 are distinctive				
p24 (13–20)	p24 (145–152)	QAISPRTL	HIV-1 infection, HIV-1 exposed seronegative	human (Cw3)	Kaul2001a
	• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers				
p24 (13–23)	p24 (145–155)	QAISPRTLNAW	HIV-1 infection	human	Betts2000
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes • 1/11 of the A2+ individuals was HLA A*0201, A1, B57 and responded to QAISPRTLNAW noted previously to be A25				
p24 (13–23)	p24 (145–155 LAI)	QAISPRTLNAW		human (A*2501)	Brander2001
	• C. Brander notes that this is an A*2501 epitope				
p24 (13–23)	p24 (145–155 SF2)	QAISPRTLNAV	HIV-1 infection	human (A25)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-A25+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 0/2 group 2, and 1/3 group 3				
p24 (13–23)	p24 (145–155 LAI)	QAISPRTLNAW		human (A5)	Kurane1998
p24 (15–23)		LSPRTLNAW	HIV-1 infection, HIV-1 exposed seronegative	human	Kaul2001c
	• This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative • The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire • ISPRTLNAW was consistently recognized by 1/22 HEPS sex worker controls (ML1250), and LSPRTLNAW was recognized by 2 additional HEPS sex worker controls (ML1693 and ML1589)				
p24 (15–23)	p24	LSPRTLNAW	HIV-1 infection	human (B*57)	Kaul2002
	• Neisseria gonorrhea cervititis in 9 HIV+ Kenyan sex workers caused a functional deficiency in IFN-gamma production in HIV-1 epitope-specific CD8+ T-cells, detected by intracellular cytokine production and tetramer assays, while not affecting the total number of epitope-specific CTLs. • Ghonorrhea caused the weaker HIV-1 specific CTL responses in 4 HIV-1 exposed persistently seronegative (HEPS) women to become undetectable by Elispot and tetramer assays, and CMV-specific CTL in 2 HEPS subjects were shown to have impaired function with regard to IFN-gamma production.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (15–23)	p24 (147–155 IIIB)	ISPRTLNAW	HIV-1 infection	human (B*5701)	Brander2001
	• C. Brander notes this is a B*5701 epitope				
p24 (15–23)		ISPRTLNAW	HIV-1 infection	human (B*5701)	Migueles2001
	• HLA B*5701 was found in a very high frequency in HIV-1 infected non-progressors, 11/13 (85%) versus 19/200 (9.5%) of progressors. Non-progressors tended to have an immune response that was highly focused on four p24 epitopes that were presented by B*5701, ISPRTLNAW, KAFSPEVIPMF, TSTLQEQIGW, and QASQEVKNW.				
p24 (15–23)		ISPRTLNAW	HIV-1 infection	human (B*5701)	Migueles2001
	• CTL activity was monitored in 27 individuals, including 10 LTNP with an over-expression of HLA B*5701 – these individuals have viral loads below the threshold of infection without therapy, and their immune response tends to be focused on peptides that contain B*5701 epitopes ISPRTLNAW, KAFSPEVIPMF, TSTLQEQIGW, and QASQEVKNW. • CTL responses are broader in B*5701+ individuals with progressive viremia than those that control viremia. • The HLA-A*0201 SLYNTVATL epitope response was not as strong individuals that carried both A2, B57.				
p24 (15–23)	Gag (147–155 LAI)	ISPRTLNAW	HIV-1 infection	human (B*5701 B*5801)	Klein1998
	• B57 has been associated with long-term non-progression in the Amsterdam cohort • The most pronounced CTL responses in HLA B*5701 LTS were to RT and Gag				
p24 (15–23)	p24 (147–155)	ISPRTLNAW	HIV-1 infection	human (B57)	Betts2000
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes • 1/11 of the A2+ individuals was HLA A*0201, A1, B57 and responded to four B57 epitopes and two others, but not SLYNTVATL				
p24 (15–23)	Gag (SF2)	ISPRTLNAW	HIV-1 infection	human (B57)	Goulder2001a
	• Epitope name: IW9 • This epitope elicited the second strongest CTL response in patient PI004 during acute infection, and maintained the response • Three CTL responses, to epitopes TSTLQEQIGW, ISPRTLNAW, and KAFSPEVIPMF, were evident early after infection; CTL responses to SLYNTVATL, QASQEVKNW, EIYKRWII, and FLKEKGGL were detectable at 5 months post-infection and beyond				
p24 (15–23)	p24 (147–155)	ISPRTLNAW	HIV-1 infection	human (B57)	Oxenius2000
	• Epitope name: ISP • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable • None of the 8 study subjects recognized this epitope but none were HLA B57+				
p24 (15–23)	p24 (15–23)	ISPRTLNAW	HIV-1 infection	human (B57)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
p24 (15–23)	p24 (147–155 SF2)	ISPRTLNAW	HIV-1 infection	human (B57)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-B57+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 0/0 group 2, and 2/2 group 3				
p24 (15–23)		ISPRTLNAW	HIV-1 infection	human (B57)	Sabbaj2002b
	• Epitope name: Gag-IW9 • Among HIV+ individuals who carried HLA B57, 2/5 (40%) recognized this epitope • Among HIV+ individuals who carried HLA B58, 0/4 (0%) recognized this epitope				
p24 (15–23)		ISPRTLNAW	HIV-1 infection	human (B57)	Oxenius2002b
	• Epitope name: ISP • Using previously defined epitopes [Oxenius2000, Oxenius2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI). • STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.				
p24 (15–23)	p24 (147–155 IIIB)	ISPRTLNAW	HIV-1 infection	human (B57, B*5801)	Goulder1996b
	• Five slow progressors made a response to this epitope, and in two it was the dominant response • Peptide defined on the basis of B*5801 binding motif, yet not cross-restricted except at high concentrations				
p24 (15–23)	p24 (subtype A)	LSPRTLNAW	HIV-1 exposed seronegative	human (B57, B58)	Kaul2000
	• 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 gamma-IFN responses in the cervix – systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses • Low risk individuals did not have such CD8+ cells • CD8+ T cell epitopes: DTVLEDINL (3 individuals), SLYNVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women				
p24 (15–23)	p24 (147–155)	LSPRTLNAW	HIV-1 infection, HIV-1 exposed seronegative	human (B57, B58)	Kaul2001a
	• Variants (L/I)SPRTLNAW are specific for the A/B clades • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure • Among HLA-B57/B58 women, 4/6 HEPS and 14/17 HIV-1 infected women recognized this epitope • The dominant response to this HLA allele was to this epitope in 2 of the 4/6 HEPS cases and in 7 of the 14/17 responsive HIV-1 infected women				
p24 (16–24)	p24	SPRTLNAWV	HIV-1 infection	chimpanzee	Santra1999
	• 3/4 animals displayed HIV-1 Gag-specific CTL activity • Effector cells from two chimpanzees were able to recognize epitopes also recognized by human HIV-1 Gag-specific CTL (SPRTLNAWV, HLA-B7, and DLNTMLNTV, HLA-B14)				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• No chimpanzee CTL were detected to the following human HIV-1 specific Gag epitopes, although they were embedded within 20mer peptides that contained a reactive epitope: ISPRTLNAW, HLA-B57; KRWIILGLNK, HLA-B27; and DRFYKTLRA, HLA-B14				
p24 (16–24)	p24 (148–156)	SPRTLNAWV		human (B*0702)	Brander2001
	• C. Brander notes this is a B*0702 epitope • Optimal peptide mapped by titration, Pers. Comm. from D. Lewinsohn to C. Brander and B. Walker				
p24 (16–24)		SPRTLNAWV	HIV-1 infection	human (B07)	Sabbaj2002b
	• Epitope name: Gag-SW9 • Among HIV+ individuals who carried HLA B07, 1/9 (11%) recognized this epitope • Among HIV+ individuals who carried HLA B81, 1/6 (17%) recognized this epitope				
p24 (16–24)	p24 (148–156)	SPRTLNAWV		human (B7)	Brander1997
	• Optimal peptide mapped by titration, Pers. Comm. from D. Lewinsohn to C. Brander and B. Walker				
p24 (16–24)	p24 (148–156)	SPRTLNAWV	HIV-1 infection	human (B7)	Brodie2000
	• Study tracks and quantifies *in vivo* migration of neo-marked CD8 HIV-specific CTL • Adoptively transferred gene-marked HIV-specific CTL homed to specific lymph node sites, colocalizing within the parafollicular regions of the lymph node adjacent to cells expressing HIV tat-fusion transcripts, indicative of viral replication • The CTL clones expressed CCR5 and localized among HIV-1 infected cells expressing MIP-1alpha and MIP-1beta, CC-chemokines produced at sites of viral replication, suggesting a possible homing mechanism • This study provides a methodology for tracking and studying antigen specific CTL *in vivo*				
p24 (16–24)	p24 (148–156)	SPRTLNAWV	HIV-1 infection, HIV-1 exposed seronegative	human (B7)	Kaul2001a
	• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure • Subject ML 1203 started with CTL responses to A*6802 DTVLEDINL and to B7 FPVTPQVPLR prior to seroconversion, and upon seroconversion acquired additional responses to A*6802 ETAYFILKL which became dominant, B7 TPGPGVIRYPL, B7 IPRRIRQGL, and B7 SPRTLNAWV				
p24 (16–24)	p24 (16–24)	SPRTLNAWV	HIV-1 infection	human (B7)	Day2001
	• The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person • Subjects with chronic HIV-1 infection recognized between 2-8 out of 11 B7-restricted epitopes • An acute seroconvertor homozygous for the B7 allele recognized five B7-restricted epitopes • The other acute seroconvertor failed to recognize any of the 11 B7-restricted epitopes tested • The B7-restricted CTL response was highly variable and there was no clearly dominant epitope				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (16–24)	p24 (16–24)	SPRTLNAWV	HIV-1 infection	human (B7)	Yu2002a
	• Epitope name: B7-SV9 • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 1/11 HLA-B7 positive individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. 1/4 individuals had detectable responses to this epitope after STI.			
p24 (16–24)	p24 (subtype B)	SPRTLNAWV	HIV-1 exposed seronegative	human (B7, B*8101)	Kaul2000
	• 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 gamma-IFN responses in the cervix – systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses • Low risk individuals did not have such CD8+ cells • CD8+ T cell epitopes: DTVLEDINL (3 individuals), SLYNVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women			
p24 (16–24)	Gag (subtype B)	SPRTLNAWV	HIV-1 exposed seronegative	human (B7, B*8101)	Rowland-Jones1998b
	• HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes • This epitope is conserved among A, B, and D clade viruses				
p24 (19–27)	p24 (151–159)	TLNAWVKVV	HIV-1 infection	human (A*02)	Huang2000
	• The single cell ELISPOT assay was optimized and highly specific, and found to work well even after the primary cells had been frozen and thawed • Increases in gamma interferon producing cells were observed in response to anti-retroviral therapy using single cell IFN-gamma-production ELISPOT • In 3/3 HLA-A*02, -B*27 subjects the immunodominant epitope was against HLA B*27 Gag p24 epitope KRWIILGL, not A2 Gag epitopes				
p24 (19–27)	p24 (151–159)	TLNAWVKVV	HIV-1 infection	human (A*02)	Rinaldo2000
	• Administration of triple-drug antiretroviral therapy (IDV, 3TC and ZDV) sometimes showed a transient increase and other times failed to increase CTL responses in patients with advanced HIV disease, but there is a stable population of tetramer stained HIV-specific CD8+ CD45RO+ cells that can persist after therapy and long periods of virus being below the level of detection				
p24 (19–27)	p24 (151–159)	TLNAWVKVV	HIV-1 infection	human (A2)	Parker1992, Parker1994
	• Study of sequence motifs preferred for peptide binding to class I HLA-A2				
p24 (19–27)	p24 (19–27)	TLNAWVKVV	HIV-1 infection	human (A2)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
p24 (19–27)	p24 (150–159)	TLNAWVKVI	HIV-1 infection, HIV-1 exposed seronegative	human (A2)	Kaul2001a
	• Variants TLNAWVKV(I/V) are A/B clade specific				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers				
p24 (19–27)	p24 (subtype B)	TLNAWVKVV	HIV-1 exposed seronegative	human (A2, A*0202)	Rowland-Jones1998b
	• HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes • This epitope is conserved among A, B and D clade viruses				
p24 (21–40)	p24 (153–172 SF2)	NAWVKVVEEKAFSPEVIPMF	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag • One of these 12 had CTL response to this peptide • The responding subject was HLA-A2, -B21				
p24 (21–40)	p24 (153–172 SF2)	NAWVKVVEEKAFSPEVIPMF	Vaccine	Rhesus macaque	Wagner1998b
	Vaccine *Vector/Type:* virus-like particle *HIV component:* gag, gp120, V3, CD4BS • A VLP is a non-infectious virus-like particle self-assembled from HIV Pr55 gag – macaques were immunized with VLPs bound to either gp120 or V3+CD4 linear domains Gag and Env specific CTL were stimulated in each case, and Ab response to gag and gp120 was elicited, but the gp120 neutralizing response occurred only with whole gp120, not V3+CD4 – despite the CTL and Ab response, immunized macaques were infected by intervenous challenge with SHIV chimeric challenge stock [Wagner1998b] • CTL specific for this epitope could be found both before and after SHIV challenge				
p24 (21–40)	Gag (153–172)	NAWVKVVEEKAFSPEVIPMF	HIV-1 infection	human (B57)	Brodie1999
	• The ability of CTL effector cells was studied by expanding autologous HIV-1 Gag-specific CTL in vitro, and adoptively transferring them • The transferred CTLs migrated to the lymph nodes and transiently reduced circulating productively infected CD4+ T cells, showing that CTL move to appropriate target sites and mediate anti-viral effects				
p24 (21–40)	p24 (153–172)	NAWVKVVEEKAFSPEVIPMF	HIV-1 infection	human (B57)	Brodie2000
	• Study tracks and quantifies *in vivo* migration of neo-marked CD8 HIV-specific CTL • Adoptively transferred gene-marked HIV-specific CTL homed to specific lymph node sites, colocalizing within the parafollicular regions of the lymph node adjacent to cells expressing HIV tat-fusion transcripts, indicative of viral replication • The CTL clones expressed CCR5 and localized among HIV-1 infected cells expressing MIP-1alpha and MIP-1beta, CC-chemokines produced at sites of viral replication, suggesting a possible homing mechanism • This study provides a methodology for tracking and studying antigen specific CTL *in vivo*				
p24 (21–42)	p24 (153–174 BH10)	NAWVKVVEEKAFSPEVIPM-FSA	HIV-1 infection	human (Bw57)	Johnson1991
	• Gag CTL response studied in three individuals				
p24 (28–36)	p24	EEKAFSPEV	HIV-1 infection	human (B*4415)	Bird2002
	• 5/233, (4 HIV-1 positive, 1 HEPS) (2.1%) Kenyan female sex workers carried the novel HLA allele B*4415. • Residues forming the B pocket of HLA B*4415 were identical to HLA B*4001, B*4402 and B*4403. These alleles preferred E, an acidic residue, at the P2 position.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The amino acid residues forming the F pocket of allele B*4415 were not correlated with other known HLA molecules, but analogy suggests a binding preference for small, neutral amino acids. • Based on the binding motif x[DE]xxxxx[VILA], 19 potential B*4415 epitopes were identified, and 1/19 was reactive in an Elispot, EEKAFSPEV.				
p24 (28–47)	p24 (160–179)	EEKAFSPEVIPMFSALSEGA	HIV-1 infection	human (B27)	Musey1997
	• Cervical and peripheral blood derived CTL clones from an HIV-infected woman recognized this epitope				
p24 (29–48)	Gag (161–180 C consensus)	EKAFSPEVPMFTALSEGAT	HIV-1 infection	human	Novitsky2002
	• HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
p24 (30–37)	p24 (162–170 LAI)	KAFSPEVI	HIV-1 infection	human (B*5703)	Brander2001
	• C. Brander notes this is a B*5703 epitope				
p24 (30–37)	p24 (30–37)	KAFSPEVI	HIV-1 infection	human (B57)	Goulder2000c
	• Two strong clonal CTL responses were generated in donor 026-BMC (HLA A3/-, B42/B57, Cw7/17) against different optimal versions of this epitope, one 8 amino acids long, one 11 • Improved stabilization of the B57-peptide complex was demonstrated by the 11 mer which fits the B57 binding motif, relative to the 8 mer, which does not • B57 tolerates marked difference in optimal peptide length – and B57 is associated with non-progressive infection				
p24 (30–37)		KAFSPEVI	HIV-1 infection	human (B57)	Sabbaj2002b
	• Epitope name: Gag-KI8 • Among HIV+ individuals tested who carried HLA B57, 0/5 (0%) recognized this epitope.				
p24 (30–40)	p24	KAFSPEVIPMF	HIV-1 infection, HIV-1 exposed seronegative	human	Kaul2001c
	• This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative • The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire • This epitope was recognized by 1/22 HEPS sex worker controls, ML1250				
p24 (30–40)	p24	KAFSPEVIPMF	HIV-1 infection	human (B*57)	Spiegel1999
	• Study examines the effect of highly active antiretroviral therapy (HAART) on HIV-1 plasma viral load, CTLp and CTLe frequencies in 8 infected children • CTLp (precursors) were measured by stimulating in culture and assaying using 51Cr release, against vaccina expressed IIIB Env, Gag, Pol, Nef, and CTLe were measured by ELISPOT • CTL against B*57-KAFSPEVIPMF was a de novo response observed in one of the children when viral load increased as a result of stopping therapy • HIV-1 specific CTL responses initially increased in children with complete viral suppression, but then decreased, suggesting viral replication is needed to maintain CTL responses				
p24 (30–40)	p24 (162–172 LAI)	KAFSPEVIPMF	HIV-1 infection	human (B*5701)	Goulder1996b
	• This peptide was recognized by CTL from five slow progressors • Peptide defined on the basis of B*5801 binding motif, yet not cross-restricted except at high concentrations				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This epitope is highly conserved				
p24 (30–40)	p24 (162–172 LAI) • C. Brander notes this is a B*5701 epitope	KAFSPEVIPMF	HIV-1 infection	human (B*5701)	Brander2001
p24 (30–40)		KAFSPEVIPMF	HIV-1 infection	human (B*5701)	Migueles2001
	• HLA B*5701 was found in a very high frequency in HIV-1 infected non-progressors, 11/13 (85%) versus 19/200 (9.5%) of progressors. Non-progressors tended to have an immune response that was highly focused on four p24 epitopes that were presented by B*5701, ISPRTLNAW, KAFSPEVIPMF, TSTLQEQIGW, and QASQEVKNW. • Attempts to make all for HLA B*5701-epitope tetramers were made, but only the HLA B*5701-KAFSPEVIPMF tetramer folded properly. The percentage of CD8+ T cells staining with this HLA B*57 gag tetramer and the fraction of CD69+IFN-+ cells responding to autologous B cells pulsed with KAFSPEVIPMF was highly correlated (r = 0.84; P = 0.005). The percent of CD8+ T cells that stain with the A*2 gag SLYNTVATL tetramer was low (0-0.31%) in a A2+ B57+ LTNP, emphasizing the focus of the immune response on the B*5701 epitopes.				
p24 (30–40)		KAFSPEVIPMF	HIV-1 infection	human (B*5701)	Migueles2001
	• CTL activity was monitored in 27 individuals, including 10 LTNP with an over-expression of HLA B*5701 – these individuals have viral loads below the threshold of infection without therapy, and their immune response tends to be focused on peptides that contain B*5701 epitopes ISPRTLNAW, KAFSPEVIPMF, TSTLQEQIGW, and QASQEVKNW. • CTL responses are broader in B*5701+ individuals with progressive viremia than those that control viremia. • The HLA-A*0201 SLYNTVATL epitope response was not as strong in individuals that carried both A2 and B57.				
p24 (30–40)	p24 (30–40)	KAFSPEVIPMF	HIV-1 infection	human (B*5701, B*5703)	Gillespie2002
	• Epitope name: KAFS • CTL responses of eight HIV+ slow progressors from Nairobi Kenya or Oxford, UK who were B*5701 or B*5703 were studied, as B*57 is associated with slow progression. • This epitope is located between the structurally conserved alpha-helix 1 and alpha-helix 2 (H1-H2) region of the p24 capsid protein, and tends to elicit strong reactions in B*57 individuals. • Broad heterogeneous cross-clade reactivity to 6 clade variants of the KAFS peptide sequence were observed in one B*5701 and 5 B*5703 HLA-restricted patients, measured by IFNγ productionElispot assays as well as tetramer binding. The clade variants were: KAFSPEVIPMF (clades A and B), kGfNpevipmf (clades A/AC); kaLspevipmf (clade A); kafspevipVf (clade A); kafNpeIipmf (group O); kafspeIipmf (A/C); kafsQevipmf (A/C); and kaLspevipmf KNFSPEVIPMF A/G). Not all variants were well recognized in all patients, for example kafsQevipmf was not able to induce IFN gamma production in 3/6 tested, and had a diminished capacity to sensitize target cells for lysis.				
p24 (30–40)	p24 (162–172 LAI) • C. Brander notes this is a B*5703 epitope	KAFSPEVIPMF	HIV-1 infection	human (B*5703)	Brander2001
p24 (30–40)		KAFSPEVIPMF	HIV-1 infection	human (B*5703)	Sabbaj2002b
	• Epitope name: Gag-KF11 • This study monitored epitope responses in HIV-1 infected minority women living in the United States • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release • Subject 00RCH59 was African American, on HAART, viral load 170, CD4 count 477 • Among HIV+ individuals who carried HLA-B57, 6/6 (100%) recognized this epitope				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (30–40)	p24 (30–40)	KAFSPEVIPMF	HIV-1 infection	human (B57)	Goulder2000c
	• Two strong clonal CTL responses were generated in donor 026-BMC (HLA A3/-, B42/B57, Cw7/17) against different optimal versions of this epitope, one 8 amino acids long, one 11 • Improved stabilization of the B57-peptide complex was demonstrated by the 11mer which fits the B57 binding motif, relative to the 8 mer, which does not • B57 tolerates marked difference in optimal peptide length – and B57 is associated with non-progressive infection				
p24 (30–40)	p24 (162–172)	KAFSPEVIPMF	HIV-1 infection	human (B57)	Betts2000
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes • 1/11 of the A2+ individuals was HLA A*0201, A1, B57 and responded to four B57 epitopes and two others				
p24 (30–40)	p24 (SF2)	KAFSPEVIPMF	HIV-1 infection	human (B57)	Goulder2000a
	• The CTL-dominant response was focused on this epitope in a HIV+ Caucasian living in Boston – this epitope is not among the most recognized peptides in the study • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK(p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa				
p24 (30–40)	Gag (SF2)	KAFSPEVIPMF	HIV-1 infection	human (B57)	Goulder2001a
	• Epitope name: KF11 • Three CTL responses in patient PI004, to epitopes TSTLQEQIGW, ISPRTLNAW, and KAFSPEVIPMF, were evident early after infection; CTL responses to SLYNTVATL, QASQEVKNW, EIYKRWII, and FLKEKGGL were detectable at 5 months post-infection and beyond				
p24 (30–40)	p24 (162–172)	KAFSPEVIPMF	HIV-1 infection	human (B57)	Oxenius2000
	• Epitope name: KAF • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable • None of the 8 study subjects recognized this epitope but none were HLA B57+				
p24 (30–40)	p24	KAFSPEVIPMF	HIV-1 infection	human (B57)	Kostense2001
	• HLA tetramers to six epitopes were used to study HLA-A2, B8 and B57 CTL in 54 patients – HIV-specific tetramer positive cells were inversely correlated with viral load in patients with high CD4, but in patients with CD4 T-cells below 400 high tetramer frequencies were found despite high viral load • Most patients have high levels of HIV-specific T-cell expansions, but many of these cells aren't functional • In 15 of the patients, the proportion of IFN gamma producing tetramer cells correlated with AIDS-free survival				
p24 (30–40)	p24 (162–172 SF2)	KAFSPEVIPMF	HIV-1 infection	human (B57)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-B57+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 0/0 group 2, and 2/2 group 3				
p24 (30–40)	p24 (163–174)	KAFSPEVIPMF	HIV-1 infection	human (B57)	Appay2000
	• Combined tetramer and intracellular cytokine staining was used to study the function of circulating CD8+ T cells specific for HIV and CMV • HIV-specific CD8+ T cells expressed lower levels of perforin than CMV-specific CD8+ T cells from the same donor, and this was associated with persistent CD27 expression on HIV-specific cells, suggesting impaired maturation • In most donors, between 50% and 95% of the activated virus-specific CD8+ T cells produced IFN-γ and MIP-1β with a distinct subset that failed to produce TNF-α				
p24 (30–40)		KAFSPEVIPMF	HIV-1 infection	human (B57)	Sabbaj2002b
	• Among HIV+ individuals who carried HLA B57, 1/5 (20%) recognized this epitope				
p24 (30–40)	p24	KAFSPEVIPMF	HIV-1 infection	human (B57)	Oxenius2002b
	• Epitope name: KAF • Using previously defined epitopes [Oxenius2000, Oxenius2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI). • STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.				
p24 (30–40)	p24 (153–164)	KAFSPEVIPMF	HIV-1 infection, HIV-1 exposed seronegative	human (B57, B58)	Kaul2001a
	• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure • Among HLA-B57/B58 women, 4/6 HEPS and 12/17 HIV-1 infected women recognized this epitope • The dominant response to this HLA allele was to this epitope in 2 of the 4/6 HEPS cases and in 7 of the 12/17 HIV-1 infected women				
p24 (30–40)	p24 (30–40)	KAFSPEVIPMF	HIV-1 infection	human (B57/B58)	Kaul2002
	• Neisseria gonorrhea cervititis in 9 HIV+ Kenyan sex workers caused a functional deficiency in IFN-gamma production in HIV-1 epitope-specific CD8+ T-cells, detected by intracellular cytokine production and tetramer assays, while not affecting the total number of epitope-specific CTLs. • Ghonorrhea caused the weaker HIV-1 specific CTL responses in 4 HIV-1 exposed persistently seronegative (HEPS) women to become undetectable by Elispot and tetramer assays, and CMV-specific CTL in 2 HEPS subjects were shown to have impaired function with regard to IFN-gamma production.				
p24 (30–40)	p24 (30–40)	KAFSPEVIPMF	HIV-1 infection	human (B58)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
p24 (31–50)	p24 (163–182)	AFSPEVIPMFSALSEGATPQ	HIV-1 infection	human	Lieberman1995
	• HIV-specific CTL lines developed by ex vivo stimulation with peptide				
p24 (31–50)	p24 (163–182 SF2)	AFSPEVIPMFSALSEGATPQ	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag • One of these 12 had CTL response to this peptide • The responding subject was HLA-A2, B21				
p24 (31–50)	p24 (163–182 SF2)	AFSPEVIPMFSALSEGATPQ	HIV-1 infection	human	Lieberman1997b
	• CTL expanded ex vivo were later infused into HIV-1 infected patients				
p24 (31–50)	p24 (SF2)	AFSPEVIPMFSALSEGATPQ	HIV-1 infection	human	Altfeld2000b
	• This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual • The response to the peptide was CD4 dependent, but the HLA presenting molecule and optimal epitope were not determined				
p24 (35–43)	p24 (167–175 LAI)	EVIPMFSAL		human (A*2601)	Goulder1996a
	• Identified as optimal epitope within Gag sequence AFSPEVIPMFSALSEGATPQ • Relatively conserved epitope within B clade and in other clades • Suspected binding motif for HLA-A26 includes T or V anchor at position 2, negative charge at position 1 • C. Brander notes that this is an A*2601 epitope in the 1999 database				
p24 (35–43)	p24 (167–175 LAI)	EVIPMFSAL		human (A*2601)	Brander2001
	• C. Brander notes that this is an A*2601				
p24 (35–43)	p24 (167–175)	EVIPMFSAL	HIV-1 infection	human (A26)	Betts2000
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes • 1/11 of the A2+ individuals that didn't respond to SLYNTVATL reacted with seven other epitopes including this epitope				
p24 (36–43)	p24 (168–175 LAI)	VIPMFSAL		human (C*0102(Cw1))	Brander2001
	• C. Brander notes this is a C*0102(Cw1) epitope				
p24 (36–43)	p24 (168–175 LAI)	VIPMFSAL		human (Cw*0102, Cw1)	Goulder1997b
p24 (36–43)	p24 (168–175)	VIPMFSAL	HIV-1 infection	human (Cw01, 02)	Betts2000
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes • 1/11 of the A2+ individuals that didn't respond to SLYNTVATL reacted with seven other epitopes including this epitope				
p24 (37–52)	Gag (169–184 LAI)	IPMFSALSEGATPQDL	HIV-1 infection	human (B12)	Buseyne1993a
	• Vertical transmission of HIV ranges from 13% to 39% • Primary assays showed cytotoxic activity against at least one HIV protein was detected in 70% of infected children • Epitopes recognized in five children were mapped using synthetic • Patient EM17 (CDC P2A+C+D2) had a CTL response to two epitopes in Gag				
p24 (37–52)	p24 (169–184 LAI)	IPMFSALSEGATPQDL	HIV-1 infection	human (B12(44))	Buseyne1993b
	• Clustering of Gag p24 CTL epitopes recognized in 29 HIV-infected people				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (37–52)	p24 (37–52)	IPMFSALSEGATPDQL	HIV-1 infection	human (B44)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
p24 (39–58)	Gag (171–190)	MFTALSEGTPQDLNTMLNT	HIV-1 infection	human	Novitsky2002
	• HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 8 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
p24 (41–60)	p24 (173–192 SF2)	SALSEGATPQDLNTMLNTVG	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag • Three of these 12 had CTL response to this peptide • The responding subjects were HLA-A3, A32, B7, B14; and HLA-A2, A3, B14, B44				
p24 (41–60)	p24 (173–192 SF2)	SALSEGATPQDLNTMLNTVG	HIV-1 infection	human	Lieberman1997b
	• CTL expanded ex vivo were later infused into HIV-1 infected patients				
p24 (41–60)	p24 (SF2)	SALSEGATPQDLNTMLNTVG	HIV-1 infection	human	Altfeld2000b
	• This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual • The response to the peptide was CD8 dependent, but the HLA presenting molecule and optimal epitope were not determined				
p24 (41–60)	p24 (179–188 subtype A)	SALSEGATPQDLNMMLNIVG	HIV-1 infection	human (B*8101)	Dorrell1999
	• CTL responses in three individuals with non-clade B infections were studied, 2 with subtype A infections, 1 with subtype C – their infections all originated in East Africa • This CTL epitope is presented by B*8101 in one of the patients with an A subtype infection – B*8101 is a newly discovered HLA allele found in Africans, and the epitope has yet to be mapped precisely • This epitope is distinct in subtype A relative to subtypes B, C, and D which share the dominant sequence: SALSEGATPQDLNTMLNTVG				
p24 (41–62)	p24 (173–194 BH10)	SALSEGATPQDLNTMLNTV-GGH	HIV-1 infection	human (B14)	Johnson1991
	• Gag CTL response studied in three individuals				
p24 (43–52)	p24 (subtype A)	LSEGATPQDL	HIV-1 infection	human (B42, B44)	Cao2000
	• HIV-1 subtypes A and D dominate the Ugandan epidemic, and a vaccine trial using B clade antigen is underway – this study addresses relative levels of cross-reactive CTL responses in Ugandans to A, D, and B clade recombinant vaccinia viruses expressing Gag, Env, Pol, RT or Nef from HIV-1 clades A, B, and D • Proteins corresponding to the subtype of the infecting strains tended to trigger higher levels of CTL response measured by percent specific lysis, but there was extensive inter-subtype cross-reactivity with B clade proteins and the co-circulating subtype • This optimal epitope sequence, recognized by CTL derived from a Ugandan with an A subtype infection (patient SP 511), is cross-reactive with subtypes A, B and D peptides				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (44–52)	p24 (176–184)	SEGATPQDL		human (B*4001)	Brander2001
	• C. Brander notes this is a B*4001, B60 epitope (Pers. Comm. A. Trocha and S. Kalams)				
p24 (44–52)	p24 (SF2)	SEGATPQDL	HIV-1 infection	human (B60(B*4001)	Altfeld2000b
	• This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes • B60 is present in 10-20% of the Caucasoid and very common in Asian populations				
p24 (44–52)	p24 (44–52)	SEGATPQDL	HIV-1 infection	human (B60/B61)	Day2001
	• No immunodominant responses were detected to five B61-restricted epitopes tested • All five B60-restricted epitopes were reactive in another subject, the strongest CTL response directed against the B60-epitope p24 SEGATPQDL, and the B60-restricted responses together contributed over one-third of the total CTL response				
p24 (46–59)	p24 (SF2)	GATPQDLNTMLNTV	HIV-1 infection	human	Goulder2000a
	• The CTL-dominant response was focused on this epitope in a HIV+ African American living in Boston with HLA A*3002/68 B14/*5802 Cw6/8 – this epitope fell within the most recognized peptides in the study • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK(p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa				
p24 (47–55)	p24 (47–55)	ATPQDLNTM	HIV-1 infection	human (B7)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
p24 (47–56)	p24 (subtype A)	ATPQDLNMML	HIV-1 exposed seronegative	human (B53)	Kaul2000
	• 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 gamma-IFN responses in the cervix – systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses • Low risk individuals did not have such CD8+ cells • CD8+ T cell epitopes: DTVLEDINL (3 individuals), SLYNVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women				
p24 (47–58)	p24 (181–192)	CTPYDINQMLNC	HIV-2 infection	human (B58)	Bertoletti1998a
	• HIV-2 epitope defined from an infection in Gambia, Bertoletti, Pers. Comm.				
p24 (48–56)	Gag (96ZM651.8)	TPQDLNTML		human (A*4201, B*8101)	Novitsky2001
	• Epitope name: G180-TL9 • This study is provides a survey of CTL responses and full length HIV-1 genome sequences from a C subtype infected Botswanan cohort • 19 of 46 (41.3%) had CTL responses to one or more peptides within the first immunodominant region of Gag (peptides TLNAWVKVIEEKAFSPEVIP, EKAFSPEVIPMFTALSEGAT, and MFTALSEGATPQDLNTMLNT), with magnitudes of response with ELISPOT results median and range 495 (103 to 1,447) SFC/10^6 PBMC • 7 of 11 HLA-A*4201+ subjects (64%) responded to peptide MFTALSEGATPQDLNTMLNT • TPQDLNTML is a A*4201 epitope within TLNAWVKVIEEKAFSPEVIP				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (48–56)	p24 (180–188 IIIB)	TPQDLNTML	HIV-1 infection	human (B*0702)	Brander2001
	• C. Brander notes this is a B*0702 epitope				
p24 (48–56)	p24 (179–187 LAI)	TPQDLNTML		human (B*4201)	Brander2001
	• C. Brander notes this is a B*4201 epitope				
p24 (48–56)	Gag (173–181 HIV-2)	TPYDINQML	HIV-2 infection	human (B*5301)	Brander2001
	• C. Brander notes this is a B*5301 epitope				
p24 (48–56)	p24 (180–188 LAI)	TPQDLNTML	HIV-1 infection	human (B*8101)	Brander2001
	• C. Brander notes this is a B*8101 epitope				
p24 (48–56)		TPQDLNTML	HIV-1 infection	human (B*8101, B*5301, B07)	Sabbaj2002b
	• Epitope name: Gag-TL9 • This study monitored epitope responses in HIV-1 infected minority women living in the United States • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release • Subjects 00RCH86 and 03RCH59 both recognized this epitope, both restricted by HLA B*8101 • Subject 00RCH86 was African American, not on HAART, viral load 51000, CD4 count 520 • Subject 03RCH59 was African American, male, on HAART, viral load 22000, CD4 count 769 • Among HIV+ individuals who carried HLA B07, 2/9 (22%) recognized this epitope • Among HIV+ individuals who carried HLA B*5301, 3/15 (20%) recognized this epitope • Among HIV+ individuals who carried HLA B81, 4/6 (67%) recognized this epitope				
p24 (48–56)	p24 (C consensus)	TPQDLNTML	HIV-1 infection	human (B42)	Goulder2000a
	• B42 and B81 are very similar, and both can present this epitope to B42-positive effector cells – this epitope is almost certainly optimal for B81 as well – B42 and or B81 are expressed in 40-45% of Zulu and Xhosa infected individuals in South Africa, and in 14/18 B42 or B81+ individuals, the dominant gag response was to TPQDLNTML • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK(p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects.				
p24 (48–56)	Gag	TPQDLNTML	HIV-1 infection	human (B42)	Goulder2000b
	• Tetramer assays were compared with three functional assays in 42 people with chronic HIV infection: ELISPOT, intracellular cytokine staining, and precursor frequency (limiting dilution assay [LDA]) • HIV-specific tetramer staining CTLs appeared to be active, and inert CTL were not found to play a significant role in chronic pediatric or adult HIV infection				
p24 (48–56)	p24	TPQDLNQML		human (B53)	Rowland-Jones1999
	• CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, and the B35 allele seems to be protective • HIV-2 sequence: TPYDINQML, no cross-reactivity, [Gotch1993]				
p24 (48–56)	Gag (173–181 HIV-2)	TPYDINQML	HIV-2 infection	human (B53)	Gotch1993
p24 (48–56)	Gag (180–188 subtype A)	TPQDLNMML	HIV-1 infection, in vitro stimulation	human (B53)	Dorrell2001
	• In vitro restimulation of CTL specific for dominant epitopes from infected individuals is possible using recombinant modified vaccinia virus Ankara (MVA) carrying A or D subtype HIV-1 Gag proteins				
p24 (48–56)	p24 (180–188 subtype A consensus)	TPQDLNMML	HIV-1 infection	human (B53)	Dorrell2001
	• In clade A infected Gambians, three HLA-B53 epitopes were defined in Gag p24 using ELISPOT, tetramer, and cytotoxicity assays • This optimal epitope was identified within the 20 mer reactive peptide that carried it by homology with a B53 epitope from HIV-2, a B subtype B7 peptide that corresponds to it, as B53 is part of the B7 superfamily, and by the proline in the anchor at position 2 • TPQDLNMML was recognized in 6/7 HLA-B53 subjects and was immunodominant in most subjects • TPQDLNMML was A subtype-specific with no cross-recognition of the subtype B, C, and D variant, TPQDLNTML, although the B/C/D variant bound more efficiently to B53 – position 7 show great positional variation in crystal structures of two HLA-B53 complexes, suggesting variation here might significantly alter the position of the peptide in the binding groove and thus affect TCR interactions • Only one subject might have had a cross-reactive response with the HIV-2 and Mamu-A*01 variant CTPYDINQML, and this subject might have been dual infected with HIV-2				
p24 (48–56)	p24 (180–188 IIIB)	TPQDLNTML	HIV-1 infection	human (B7)	Wilson1999a
	• This study describes maternal CTL responses in the context of mother-to-infant transmission • Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants • No variants of this epitope were found in a non-transmitting mother that had a CTL response to this epitope				
p24 (48–56)	p24 (180–188)	TPQDLNTML	HIV-1 infection	human (B7)	Jin2000b
	• This is the optimal epitope for the immunodominant response defined using a conventional approach in an HLA B7+ long-term non-progressor • Three additional sub-dominant HLA B7 epitopes were defined using EpiMatrix, a non-anchor based strategy for defining potential epitopes, which highlighted 2078 possible epitopes in the autologous HIV-1 derived from the study subject – this was followed by B7 anchor residue prediction which narrowed the set to 55 peptides, three of which could serve as functional CTL epitopes				
p24 (48–56)	p24 (SF2)	TPQDLNTML	HIV-1 infection	human (B7)	Goulder2001a
	• Epitope name: TL9 • Recognized by patient 9354 during chronic infection, used as a positive control in a study of the SLYNTVATL epitope				
p24 (48–56)	p24 (48–56)	TPQDLNTML	HIV-1 infection	human (B7)	Day2001
	• The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person • Subjects with chronic HIV-1 infection recognized between 2-8 out of 11 B7-restricted epitopes				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• An acute seroconvertor homozygous for the B7 allele recognized five B7-restricted epitopes • The other acute seroconvertor failed to recognize any of the 11 B7-restricted epitopes tested • The B7-restricted CTL response was highly variable and there was no clearly dominant epitope				
p24 (48–56)	p24 (48–56)	TPQDLNTML	HIV-1 infection	human (B7)	Yu2002a
	• Epitope name: B7-TL9 • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 1/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. 1/4 individuals had detectable responses to this epitope after STI.				
p24 (48–56)	p24	TPQDLNTML	HIV-1 infection	human (B7)	Altfeld2002
	• Epitope name: B7-TL9(p24) • Peripheral blood (PB) and lymph node (LN) CD8+ T-cell responses were compared in 15 asymptomatic HIV-1 infected patients using all known optimal CTL epitopes (http://hiv-web.lanl.gov/content/hiv-db/REVIEWS/brander2001.html) for each person's class I HLA alleles. • 60 epitope responses were detected in both PB and LN samples of the 15 patients, and an additional 8 responses were detected only in LN. The total magnitude of the response was similar in LN and PB, but the percentage of CD8+ T cells in the LN is lower so the number of HIV-specific cells per million CD8+ T-cells is higher in the LN. • 1 year post-HAART treatment in five patients studied, the magnitude of the CD8 T-cell response was decreased in both LN and PB, but more dramatically in PB, and 13/25 epitope responses in the PB became undetectable, in contrast to 5/26 in the LN. • Treatment interruption following HAART induced resulted in increased viremia accompanied by the restoration of the detection of 13 epitopes that had become undetectable in the PB, and the addition of 9 novel epitope responses. • Breakdowns of epitope responses were shown for 4 individuals. Patient A displayed the greatest response to epitope B14-EL9(gp41), a strong response to B7-TL9(p24), and responses to B7-TM9(Nef) and A32-PW10(RT).				
p24 (48–56)	p24 (180–188 LAI)	TPQDLNTML	HIV-1 infection	human (C*0802(Cw8))	Brander2001
	• C. Brander notes this is a C*0802(Cw8) epitope				
p24 (48–57)	Gag	TPQDLNMMLN		human (B7)	De Groot2001
	• The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes • A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes were identified that could stimulate IFNγ production in an ELISPOT assay • TPQDLNMMLN was newly defined as an HLA-B7 epitope in this study, athough it was previously published as a B*8101 epitope • TPQDLNMMLN was shown to stimulate an ELISPOT response, but could not be shown to bind to HLA-B7 • The variant TPQDLNTMLN was cross-reactive, had previously been identified as a HLA-B14 epitope, and could bind to HLA-B7				
p24 (49–57)	p24 (181–189 LAI)	PQDLNTMLN	HIV-1 infection	human (B14, Cw8)	Lubaki1997
	• Eighty two HIV-1-specific CTL clones from 5 long-term non-progressors were isolated and analyzed for breadth of response • A sustained Gag, Env and Nef response was observed, and clones were restricted by multiple HLA epitopes, indicating a polyclonal response • Despite this being a well defined conserved epitope, none of the 11 gag-specific clones from a B-14 positive subject could recognize either it or p24 RAEQASQEV • Christian Brander notes that B14 and Cw8 are in linkage disequilibrium, and that this epitope may be Cw8				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (51–59)	p24	DLNTMLNTV	HIV-1 infection	chimpanzee	Santra1999
	• 3/4 animals displayed HIV-1 Gag-specific CTL activity • Effector cells from two chimpanzees were able to recognize two epitopes also recognized by human HIV-1 Gag-specific CTL (SPRTLNAWV, HLA-B7, and DLNTMLNTV, HLA-B14) • No chimpanzee CTL were detected to the following human HIV-1 specific Gag epitopes, although they were embedded within 20mer peptides that contained a reactive epitope: ISPRTLNAW, HLA-B57; KRWIILGLNK, HLA-B27; and DRFYKTLRA, HLA-B14				
p24 (51–59)	p24 (subtype A)	DLNMMLNIV	HIV-1 exposed seronegative	human (B14)	Kaul2000
	• 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 gamma-IFN responses in the cervix – systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses • Low risk individuals did not have such CD8+ cells • CD8+ T cell epitopes: DTVLEDINL (3 individuals), SLYNVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women				
p24 (51–59)	p24	DLNMMLNIV	HIV-1 infection	human (B14)	Kaul2001c
	• This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative • The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire • This epitope was recognized in 1/22 HEPS sex worker controls, ML1792				
p24 (51–59)	p24 (183–191 LAI)	DLNTMLNTV	HIV-1 infection	human (B14)	Mollet2000
	• Epitope name: G5 • A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses • In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished • Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change				
p24 (51–59)	p24 (183–191)	DLNMMLNIV	HIV-1 infection, HIV-1 exposed seronegative	human (B14)	Kaul2001a
	• Variants DLNMMLNIV/DLNTMLNVV are specific for clades A/B • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure • Among HLA-B14 women, 4/4 HEPS and 3/7 HIV-1 infected women recognized this epitope, likelihood ratio 4.8, p value 0.1, and HEPS women tended to respond to DLNMMLNIV/DLNTMLNVV, while infected women tended to respond to DRF(F/W)KTLRA • The dominant response to this HLA allele was to this epitope for all 4/4 HEPS cases and in only one of the 3/7 HIV-1 infected women • Differences in epitope specificity were only seen for responses restricted by class I HLA alleles A2, A24, A*6802, B14, and B18, previously shown to be associated with resistance to HIV-1 in this cohort				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Four epitopes were considered to be "resistant epitopes", as they were preferentially reactive in HEPS women and so may confer resistance, and these were found in three different proteins: A2 ILK(D/E)PVHGV in RT, A*6802 DTVLEDINL in Protease, B14 DLN(M/T)LN(I/V)V in p24 and B18 FRDYVDRF(Y/F)K also in p24				
p24 (51–59)	p24	DLNMMLNIV	HIV-1 infection	human (B14)	Kaul2002
	• Neisseria gonorrhea cervititis in 9 HIV+ Kenyan sex workers caused a functional deficiency in IFN-gamma production in HIV-1 epitope-specific CD8+ T-cells, detected by intracellular cytokine production and tetramer assays, while not affecting the total number of epitope-specific CTLs. • Ghonorrhea caused the weaker HIV-1 specific CTL responses in 4 HIV-1 exposed persistently seronegative (HEPS) women to become undetectable by Elispot and tetramer assays, and CMV-specific CTL in 2 HEPS subjects were shown to have impaired function with regard to IFN-gamma production.				
p24 (51–59)	p24 (183–191 LAI)	DLNTMLNTV	HIV-1 infection	human (B14, Cw8)	Johnson1992, Nixon1988
	• Recent evidence indicates this is a Cw8 epitope; B14 and Cw8 are in linkage disequilibrium and the HLA presenting molecule is hard to distinguish (P. Goulder, personal communication)				
p24 (51–59)	p24	DLNTMLNTV	HIV-1 exposed seronegative	human (B14, Cw8)	Rowland-Jones1998a
	• A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating • The A subtype consensus is identical to the B clade epitope • The D subtype consensus is dLNmMLNiV • Recent evidence indicates this is a Cw8 epitope;B14 and Cw8 are in linkage disequilibrium and the HLA presenting molecule is hard to distinguish (P. Goulder, personal communication)				
p24 (51–59)	p24 (183–191 LAI)	DLNTMLNTV	HIV-1 infection	human (C*0802)	Brander2001
	• C. Brander notes this is a C*0802 epitope				
p24 (51–59)	p24 (183–191 LAI)	DLNTMLNTV	HIV-1 infection	human (Cw8)	McMichael1994
	• Review of HIV CTL epitopes – defined by B14 motif found within a larger peptide • Recent evidence indicates this is a Cw8 epitope;B14 and Cw8 are in linkage disequilibrium and the HLA presenting molecule is hard to distinguish (P. Goulder, personal communication)				
p24 (51–59)	p24 (subtype B)	DLNTMLNTV	HIV-1 exposed seronegative	human (Cw8, B*1402)	Rowland-Jones1998b
	• HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes • This epitope is conserved among B and D clade viruses • The Clade A version of the epitope, DLNNMLNIV, was preferentially recognized by CTL • Recent evidence indicates this is a Cw8 epitope;B14 and Cw8 are in linkage disequilibrium and the HLA presenting molecule is hard to distinguish (P. Goulder, personal communication)				
p24 (51–70)	p24 (183–202 SF2)	DLNTMLNTVGGHQAAMQMLK	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag • One of these 12 had CTL response to this peptide • The responding subject was HLA-A26, A30, B38				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (51–82)	Gag (183–214 LAI)	DLNTMLNTVGGHQAAMQML-KETINEEAAEWDR	Vaccine	human	Gahery-Segard2000
	Vaccine *Vector/Type:* lipopeptide *HIV component:* six peptides • Anti-HIV lipopeptide vaccine consisting of six long amino acid peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial • A CD4+ T cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 2/10 reacted to this peptide • 9/12 tested mounted a CTL response to at least one of the six peptides; each of the six peptides elicited a CTL response in at least one individual • None of the 12 tested had an IgG response to this peptide				
p24 (61–69)	p24 (193–201 LAI)	GHQAAMQML		human (B*3901)	Brander2001
	• C. Brander notes this is a B*3901 epitope				
p24 (61–69)	p24 (193–201 LAI)	GHQAAMQML		human (B39)	Kurane1998
	• Optimal peptide defined by titration				
p24 (61–71)	p24 (193–203 BRU)	GHQAAMQMLKE	HIV-1 infection	human (A2)	Claverie1988
	• One of 4 epitopes first predicted, then shown to stimulate HLA-A2 restricted CTL line				
p24 (61–80)	p24 (193–212 SF2)	GHQAAMQMKETINEEAAEW	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag • One of these 12 had CTL response to this peptide • The responding subject was HLA-A26, A30, B38				
p24 (61–82)	p24 (193–214 BH10)	GHQAAMQMLKETINEEAAE-WDR	HIV-1 infection	human (Bw52)	Johnson1991
	• Gag CTL response studied in three individuals				
p24 (62–70)	p24 (194–202 LAI)	HQAAMQMLK		human (B52)	Brander1996b
	• P. Goulder, pers. comm.				
p24 (65–73)	Gag (199–207 HXB2)	AMQMLKETI	Vaccine	murine (H-2^d)	Qiu1999
	Vaccine *Vector/Type:* DNA *Strain:* HXB2 *HIV component:* gag • Different expression vectors were tested to increase Gag expression in cell lines and create suitable vectors for DNA vaccines • Stable Gag expression was achieved in murine p815 cells, using a Gag gene that had mutated silent base positions that disrupt inhibitory RNA sequences which promote RNA degradation • Silent mutations were more effective than introduction of the D retrovirus cis-acting posttranscriptional control element (CTE) for enhancing Gag expression • The gag vector with silent mutations given as a vaccine to BALB/c mice gave CTL responses in splenic mononuclear cells, using peptide pulsed cells as targets				
p24 (65–73)	p24 (199–207 SF2)	AMQMLKETI	Vaccine	murine (H-2^d)	Neidleman2000
	Vaccine *Vector/Type:* protein, vaccinia *Strain:* SF2 *HIV component:* soluble Gag, or GagPol expressing vaccinia *Adjuvant:* heat-labile enterotoxin (LT) from E. coli • Epitope name: p7g				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Intranasal immunization of CB6F1 (H2bxd) mice with soluble gag p55 with LT ADP-ribosyltransferase mutants (LTK63 and LTK73) from Escherichia coli as adjuvants was tested • Intranasal and intramucosal immunization of p55 gag protein with LTK63 or LTK72 adjuvant induced a CTL response comparable to intramuscular immunization responses • Oral co-administration of LTR72, with residual ADP-ribosyltransferase activity, induced systemic CTL responses, but LTK63 with no ADP-ribosyltransferase activity did not				
p24 (65–73)	p24 (66–74)	AMQMLKETI	Vaccine	murine (H-2^d)	Marsac2002
	Vaccine *Vector/Type:* DNA *HIV component:* Gag *Adjuvant:* vesicular stomatitis virus glycoprotein (VSV-G) • BALB/c mice were injected with plasmids expressing HIV-1 Gag with or without coinjection of a plasmid expressing vesicular stomatitis virus glycoprotein (VSV-G). The combination encodes VSV-G pseudotyped Gag particles that can be taken up by cells for presentation in either the class I or class II pathways, while exogenous Gag alone can only be taken into the class II pathway. • Vaccination with DNA expressing VSV-G pseudotyped Gag particles rather than just Gag increase Gag-specific CTL responses generally as well as the specific H-2d restricted anti-AMQMLKETI response.				
p24 (65–73)	Gag (p24) (199–207 SF2)	AMQMLKETI	Vaccine	murine (H-2^{kd})	O'Hagan2002
	Vaccine *Vector/Type:* recombinant protein *Strain:* SF2 *HIV component:* Gag p55 *Adjuvant:* CpG, MF59, DOTAP, DDA, PLG-microparticle, urea • Epitope name: p7G • Intramuscular or intraperitoneal immunization of BALB/c or CB6F1 mice with urea-solubilized, emulsified, or PLG-microparticle associated p55 Gag was studied in conjunction with the adjuvant CpG. CpG did not enhance CTL immunity when combined with urea solubilized p55, but did when combined with emulsions and PLG-microparticle antigen. • CpG shifted the Ab response towards a IgG2a, and CpG was shown to upregulate CD86 on mouse bone-marrow derived dendritic cells.				
p24 (65–73)	p24 (199–207 SF2)	AMQMLKETI	Vaccine	murine (H-2K^d)	Doe1997
	Vaccine *Vector/Type:* vaccinia *HIV component:* Gag, Pol • Immunodominant murine CTL response to this peptide observed after immunization with vaccine VVgagpol • Optimal peptide was defined				
p24 (65–73)	Gag (197–205)	AMQMLKETI	Vaccine	murine (H-2K^d)	Rayevskaya2001
	Vaccine *Vector/Type:* Listeria monocytogenes *HIV component:* gag • BALB/c mice were immunized with a highly attenuated recombinant Listeria monocytogenes, Lmdaldat, that can grow only when supplemented with D-alanine, and that expresses HIV-1 HXB2 Gag • Parenteral immunization provided protection against systemic and mucosal challenges with a recombinant vaccinia virus expressing HIV-1 gag, and a long lasting memory CTL response against Gag in spleen, mesenteric lymph nodes, and Peyer's patches directed against the gag protein • Oral immunization gave protection only against mucosal virus challenge and was associated with a transient CTL response in the three lymphoid tissues examined • L. monocytogenes is a gram-positive bacteria that enters the macrophage on phagocytosis and lives in the cytoplasm – secreted L. monocytogenes antigens are processed and presented by both class I and class II pathways				
p24 (65–73)	Gag (197–205 SF2)	AMQMLKETI	Vaccine	murine (H-2K^d)	Mata1998
	Vaccine *Vector/Type:* Listeria monocytogenes *Strain:* HXB2 *HIV component:* Gag • BALB/c mice were immunized with recombinant Listeria monocytogenes (Lm-Gag) expressing HIV-1 HXB2 Gag				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• L. monocytogenes is a gram-positive bacteria that enters the macrophage on phagocytosis and lives in the cytoplasm – secreted L. monocytogenes antigens are processed and presented by both class I and class II pathways • This is the immunodominant CTL epitope in Gag in BALB/c mice • AMQMLKETI does not contain established Kd anchoring residue in position 2, tyrosine or phenylalanine, thus deviating from the typical Kd anchoring motif – the lack of the aromatic anchor residue is compensated for by interaction of the glutamine at P3 with pocket D of Kd				
p24 (65–73)	Gag (HXB2)	AMQMLKETI	Vaccine	murine (H-2K^d)	Haglund2002a
	Vaccine *Vector/Type:* vesicular stomatitis virus (VSV), vaccinia *Strain:* Env, IIIB; Gag HXB2 *HIV component:* Gag, Env • BALB/c mice were vaccinated with rec vesicular stomatitis virus (rVSV) expressing either HIV-1 Gag, Env, or both, and compared to using rec Env and Gag in vaccinia virus (rVVs). The primary response was determined by cell lysis, cytokine production and tetramer staining. • Primary CTL responses to the immunodominant Gag (AMQMLKETI) epitope peaked in 7 days for GAG-rVSV, 3% of the cells were tetramer positive, and this response was 8-fold higher than for Gag-rVV. • Vaccinating with GagEnv-rVSV carrying both Gag and Env allowed recognition of both HIV-1 proteins, but at reduced levels compared to either Gag-rVSV or Env-rVSV alone. • Intranasal immunization with Env-rVSV yielded CTL responses that were strong but reduced compared to an intraperitoneal route.				
p24 (65–73)	Gag (HXB2)	AMQMLKETI	Vaccine	murine (H-2K^d)	Haglund2002b
	Vaccine *Vector/Type:* vesicular stomatitis virus (VSV), vaccinia *Strain:* Env, IIIB; Gag HXB2 *HIV component:* Gag, Env • BALB/c mice were vaccinated with rec vesicular stomatitis virus (rVSV) expressing either HIV-1 Gag or Env, or both, and retention of memory responses and recall responses were studied by tetramer staining and IFN-gamma production. • Seven months after vaccination with Env-rVSV, 6% of the CD8+ cells were tetramer positive for the immunodominant Env epitope; these cells had a memory phenotype, CD44-Hi positive. • Env in rec vaccinia virus (Env-rVV) elicited a strong recall response, with up to 45% to the CD8+ T-cell population tetramer positive and activated (expressing CD62L-Lo), and capable of IFN-gamma production. • A prime with Env-rVSV and heterologous boost of Env-rVV gave remarkably high levels of memory cells, with approximately 1/3 of the CD8+ splenocytes being Env specific memory cells 150 days after the boost. • A Gag-rVSV or EnvGag-rVSV prime and with a heterologous Gag-rVV or EnvGag-rVV boost combination gave 40% tetramer positive CD8+ cells, but the fraction of IFN-gamma producing cells was only about 25%. Still the heterologous vector prime-boost combination showed a profound benefit. • A HIV-1 protein rVSV prime, rVV boost was a more potent combination than a vector reversal of a rVV prime and rVSV boost.				
p24 (69–86)	Gag (201–218 LAI)	LKETINEEAAEWDRVPV	HIV-1 infection	human	Buseyne1993a
	• Vertical transmission of HIV ranges from 13% to 39% • Primary assays showed cytotoxic activity against at least one HIV protein was detected in 70% of infected children • Epitopes recognized in five children were mapped using synthetic peptides and secondary cultures • Patient EM28 (CDC P2A) had a CTL response to four epitopes in Gag				
p24 (70–78)		KETINEEAA	HIV-1 infection	human (B*4002)	Sabbaj2002b
	• Epitope name: Gag-KA9 • This study monitored epitope responses in HIV-1 infected minority women living in the United States • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release • This epitope was newly defined in this study • Patient 01RCH46 was Hispanic, on HAART, and had a viral load of 21000 and CD4 count of 623 – she also recognized GELDRWEKI, p17(11-19), HLA B*4002, and TAFTIPSI, RT(128-135), HLA A*0217				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Among HIV+ individuals who carried HLA B40, 3/5 (60%) recognized this epitope				
p24 (71–80)	p24 (203–212)	ETINEEAAEW	HIV-1 infection	human (A*2501)	Klenerman1996
	• The epitope was defined through direct stimulation of PBMC with 20-mer peptides • It is in a conserved region, ETINEEAAEW is found in most B, D, and E subtype isolates • DTINEEAAEW is found in A and some D subtype sequences				
p24 (71–80)	p24 (203–212)	ETINEEAAEW	HIV-1 infection	human (A*2501)	Brander2001
	• C. Brander notes this is an A*2501 epitope				
p24 (71–80)	p24 (203–212)	ETINEEAAEW	HIV-1 infection	human (A*2501)	vanBaalen1996
	• Conserved between B and D subtypes, variable in other clades; a consensus of clades A,C, F, G, and H and a peptide of HIV-2ROD over this region were not recognized by CTL recognizing the index peptide • C. Brander notes that this is an A*2501 epitope in the 1999 database				
p24 (71–80)	p24	ETINEEAAEW		human (A25)	Rowland-Jones1999
	• CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5 • In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, and the B35 allele seems to be protective • HIV-2 sequence: EIINEEAAEW, no cross-reactivity [vanBaalen1996]				
p24 (71–80)	p24 (203–212 SF2)	ETINEEAAEW	HIV-1 infection	human (A25)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-A25+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 0/2 group 2, and 1/3 group 3				
p24 (71–80)		DTINEEAAEW	HIV-1 infection	human (B*5301)	Sabbaj2002b
	• Epitope name: Gag-DW10 • Among HIV+ individuals who carried HLA B*5301, 2/15 (13%) recognized this epitope				
p24 (71–80)		ETINEEAAEW	HIV-1 infection	human (B*5301)	Sabbaj2002b
	• Epitope name: Gag-EW10 • Among HIV+ individuals who carried HLA B*5301, 2/15 (13%) recognized this epitope				
p24 (71–80)	p24 (203–212)	DTINEEAAEW	HIV-1 infection, HIV-1 exposed seronegative	human (B53)	Kaul2001a
	• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure • Among HLA-B53 women, 0/2 HEPS and 7/9 HIV-1 infected women recognized this epitope • The dominant response to this HLA allele was to this epitope in 4 of the 7/9 responsive HIV-1 infected women				
p24 (71–80)	p24 (203–212 subtype A consensus)	DTINEEAAEW	HIV-1 infection	human (B53)	Dorrell2001
	• In clade A infected Gambians, three HLA-B53 epitopes were defined in Gag p24 using ELISPOT, tetramer, and cytotoxicity assays • Two of the new epitopes lacked the predicted by P2 anchors, DTINEEAAEW and QATQEVKNM, and bound to B53 with high affinity, thus extending the anchor residue motif for B53 and the related B35 • Two overlapping 20 mer peptides carry this complete epitope, but only one stimulates recognition, which could be due to different peptide processing • DTINEEAAEW was recognized in only 2/7 HLA-B53 subjects • DTINEEAAEW was not A subtype specific and there was cross-recognition although diminished, of the subtype B, C, and D variant, ETINEEAAEW • In one of the two subjects there was cross-recognition of the HIV-2 version of the epitope, EIINEEAADW				
p24 (71–90)	p24 (203–222 SF2)	ETINEEAAEWDRVHPVVHA-GP	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag • One of these 12 had CTL response to this peptide • The responding subject was HLA-A2, B21				
p24 (78–86)		AEWDRVHPV	HIV-1 infection	human (B*4002)	Sabbaj2002b
	• Epitope name: Gag-AV9 • This study monitored epitope responses in HIV-1 infected minority women living in the United States • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release • This epitope was newly defined in this study • Patient 01RCH59 was Hispanic, not on HAART, and had a viral load of 5100 and CD4 count of 349 – she also recognized TERQANFL, p2p7p1p6(64-71), HLA-B*4002, and KEKGGLEGL, Nef(92-100), HLA-B*4002 • Among HIV+ individuals who carried HLA B40, 4/5 (80%) recognized this epitope				
p24 (83–92)	p24 (215–223 IIIB)	VHPVHAGPIA	HIV-1 infection	human (B55)	Sipsas1997
	• HIV IIIB proteins were used to define the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB • LHPVHAGPVA, a variant found in HIV-1 PH136, was also recognized • LHPVHAGPIA, a variant found in HIV-1 RF, was also recognized • LHPVHAGPIT, a variant found in HIV-1 MN, was also recognized • LHPAQAGPIA, a variant found in HIV-1 JH3, was recognized at high peptide concentrations				
p24 (84–92)	p24 (84–92)	HPVHAGPIA	HIV-1 infection	human (B7)	Yu2002a
	• Epitope name: B7-HA9 • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• 1/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection—10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. 3/4 individuals had detectable responses to this epitope after STI.				
p24 (87–101)	Gag (219–233 LAI)	HAGPIAPGQMREPRG	HIV-1 infection	human	Buseyne1993a
	• Vertical transmission of HIV ranges from 13% to 39% • Primary assays showed cytotoxic activity against at least one HIV protein was detected in 70% of infected children • Epitopes recognized in five children were mapped using synthetic peptides and secondary cultures • Patient EM28 (CDC P2A) had a CTL response to four epitopes in Gag				
p24 (87–101)	p24 (219–233 BRU)	HAGPIAPGQMREPRG	HIV-1 infection	human (A2)	Claverie1988
	• One of 4 epitopes predicted then shown to stimulate HLA-A2 restricted CTL line				
p24 (91–110)	p24 (223–242 SF2)	IAPGQMREPRGSDIAGTTST	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag • One of these 12 had CTL response to this peptide • The responding subject was HLA-A2, A24, B13, B35				
p24 (101–120)	p24 (233–252 SF2)	GSDIAGTTSTLQEQIGWMTN	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag • One of these 12 had CTL response to this peptide • The responding subject was HLA-A26, A30, B38				
p24 (107–115)	Gag (239–247 SF2)	TTSTLQEQI	Vaccine	murine (H-2K^d)	Mata1998
	Vaccine *Vector/Type:* Listeria monocytogenes *Strain:* HXB2 *HIV component:* Gag • BALB/c mice were immunized with recombinant Listeria monocytogenes (Lm-Gag) expressing HIV-1 HXB2 Gag • L. monocytogenes is a gram-positive bacteria that enters the macrophage on phagocytosis and lives in the cytoplasm – secreted L. monocytogenes antigens are processed and presented by both class I and class II pathways				
p24 (108–117)		TSTLQRQIGW	HIV-1 infection	human	Kaul2001c
	• This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative • The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire • This epitope was recognized in 1/22 HEPS sex worker controls (ML1250)				
p24 (108–117)		TSTLQEQIGW	HIV-1 infection	human (B*5701)	Migueles2001
	• HLA B*5701 was found in a very high frequency in HIV-1 infected non-progressors, 11/13 (85%) versus 19/200 (9.5%) of progressors. Non-progressors tended to have an immune response that was highly focused on four p24 epitopes that were presented by B*5701, ISPRTLNAW, KAFSPEVIPMF, TSTLQEQIGW, and QASQEVKNW.				
p24 (108–117)		TSTLQEQIGW	HIV-1 infection	human (B*5701)	Migueles2001
	• CTL activity was monitored in 27 individuals, including 10 LTNP with an over-expression of HLA B*5701 – these individuals have viral loads below the threshold of infection without therapy, and their immune response tends to be focused on peptides that contain B*5701 epitopes ISPRTLNAW, KAFSPEVIPMF, TSTLQEQIGW, and QASQEVKNW.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• CTL responses are broader in B*5701+ individuals with progressive viremia than those that control viremia. • The HLA-A*0201 SLYNTVATL epitope response was not as strong individuals that carried both A2, B57.				
p24 (108–117)	p24 (241–250 LAI) • C. Brander notes this is a B*5801 epitope	TSTVEEQQIW	HIV-2 infection	human (B*5801)	Brander2001
p24 (108–117)	p24 (240–249 LAI) • C. Brander notes this is a B*5801 epitope	TSTLQEQIGW	HIV-1 infection	human (B*5801)	Brander2001
p24 (108–117)	p24 (233–252) • This study focuses on six rare long-term survivor HIV-infected people who were infected for many years without exhibiting immune dysregulation – such immunologically normal HIV-infected (INHI) cases occur at a frequency between 0.1 and 1% in the infected population • No direct CTL were found in any of the six INHIs, but above background CTLp activity was founded in 3/6 INHIs • Epitope sequences were deduced from larger reactive peptides based on HLA binding motifs – XSXXXXXXXW is a B57 binding motif, and CTL activity against TSTLQEQIGW has been found in two other B57 long-term non-progressors	TSTLQEQIGW	HIV-1 infection	human (B57)	Bernard1998
p24 (108–117)	Gag (SF2) • Epitope name: TW10 • Dominant epitope in acute infection in patient PI004, who did not receive any antiviral therapy • 1-2 months post seroconversion, subject PI004 displayed a significant decrease in TW10 peptide recognition, followed by an increased CTL response against epitope SL9, SLYNTVATL and other epitopes • Three CTL responses, to epitopes TSTLQEQIGW, ISPRTLNAW, and KAFSPEVIPMF, were evident early after infection; CTL responses to SLYNTVATL, QASQEVKNW, EIYKRWII, and FLKEKGGL were detectable at 5 months post-infection and beyond	TSTLQEQIGW	HIV-1 infection	human (B57)	Goulder2001a
p24 (108–117)	p24 (108–117) • Epitope name: TST • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable • None of the 8 study subjects recognized this epitope but none were HLA B57+	TSTLQEQIGW	HIV-1 infection	human (B57)	Oxenius2000
p24 (108–117)	p24 (108–117) • One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles	TSTLQEQIGW	HIV-1 infection	human (B57)	Ferrari2000
p24 (108–117)	p24 • Neisseria gonorrhea cervititis in 9 HIV+ Kenyan sex workers caused a functional deficiency in IFN-gamma production in HIV-1 epitope-specific CD8+ T-cells, detected by intracellular cytokine production and tetramer assays, while not affecting the total number of epitope-specific CTLs. • Ghonorrhea caused the weaker HIV-1 specific CTL responses in 4 HIV-1 exposed persistently seronegative (HEPS) women to become undetectable by Elispot and tetramer assays, and CMV-specific CTL in 2 HEPS subjects were shown to have impaired function with regard to IFN-gamma production.	TSTLQEQIGW	HIV-1 infection	human (B57)	Kaul2002
p24 (108–117)	p24 • Epitope name: TST • Using previously defined epitopes [Oxenius2000, Oxenius2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI).	TSTLQEQIGW	HIV-1 infection	human (B57)	Oxenius2002b

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.				
p24 (108–117)	p24 (235–243)	TSTLQEQIGW	HIV-1 infection, HIV-1 exposed seronegative	human (B57, B58)	Kaul2001a
	• TSTLQEQIGW cross reacts with both for the A and B clades • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers				
p24 (108–117)	p24 (241–250)	TSTVEEQQIW	HIV-2 infection	human (B58)	Bertoletti1998a
	• HIV-2 epitope defined from an infection in Gambia, Bertoletti, Pers. Comm. • All HIV-2 sequences from the database are TSTVEEQIQW in this region, not TSTVEEQQW as in the paper				
p24 (108–117)	p24	TSTLQEQIGW	HIV-1 exposed seronegative	human (B58)	Rowland-Jones1999
	• CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5 • In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, and the B35 allele seems to be protective • HIV-2 sequence: TSTVEEQIQW, CTL are cross-reactive, [Bertoletti1998b]				
p24 (108–117)	p24 (240–249)	TSTLQEQIGW	HIV-2 infection	human (B58)	Bertoletti1998b
	• CTL responses in HLA-B*5801 positive HIV-2 infected individuals have a dominant response to Gag and tolerate extensive substitution, thus HLA-B*5801+ individuals may have an enhanced potential for cross-protection between HIV-1 and HIV-2 • This can be an immunodominant epitope in HLA-B57 and B*5801 infected individuals, and is associated with long-term non-progression [Goulder1996b] • HIV-2 sequence: HIV-2 ROD has the epitope sequence TSTVEEQIQW, and the CTL from a person infected with HIV-2 was cross-reactive with HIV-1 epitopes • The epitope is TSTLQEQIGW in HIV-1 B clade, and TSTVEEQIQW in HIV-2 ROD • HLA B*5801 and B35 may preferentially select HIV-1 and HIV-2 cross-reactive epitopes				
p24 (108–117)	p24 (240–249 SF2)	TSTLQEQIGW	HIV-1 infection	human (B58)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-B58+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 1/1 group 2, and 0/0 group 3				
p24 (108–117)	p24 (108–117)	TSTLQEQIGW	HIV-1 infection	human (B58)	Goulder2001c
	• Epitope name: TW10 • Responses to this dominant A3-restricted Gag epitope are present during the time of decreasing viral load in acute infection • Mutations in this epitope were observed in autologous clones of subjects who were B58-positive with a higher frequency than those who were B58-negative (P = 0.02) • These mutations are being sexually transmitted in adult infections				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (108–118)	p24 (240–249 LAI)	TSTLQEQIGWF	HIV-1 infection	human (B*57, B*5801)	Goulder1996b
	• Response to this epitope was found in 4 slow progressing HLA-B*57 individuals, in 2 it was dominant or very strong • For one donor (from Zimbabwe) this was defined as the optimal peptide • This epitope can be presented in the context of the closely related HLA molecules B*5801 and B*57				
p24 (108–118)	p24 (240–249 LAI)	TSTLQEQIGWF	HIV-1 infection	human (B*5701)	Brander2001
	• C. Brander notes this is a B*5701 epitope				
p24 (108–118)		TSTLQEQIGWF	HIV-1 infection	human (B57)	Sabbaj2002b
	• Epitope name: Gag-TF11 • Among HIV+ individuals who carried HLA B57, 2/5 (40%) recognized this epitope				
p24 (109–117)	Gag (241–249 LAI)	STLQEQIGW	HIV-1 infection	human (B*5701 B*5801)	Klein1998
	• B57 has been associated with long-term non-progression in the Amsterdam cohort • The most pronounced CTL responses in HLA B*5701 LTS were to RT and Gag				
p24 (109–117)		STLQEQIGW	HIV-1 infection	human (B57)	Sabbaj2002b
	• Epitope name: Gag-SW9 • Among HIV+ individuals who carried HLA B57, 1/5 (20%) recognized this epitope • Among HIV+ individuals who carried HLA B58, 1/4 (25%) recognized this epitope				
p24 (118–126)	Gag (282–290)	MTNNPPIPV	HIV-1 infection	human (A2 supertype)	Propato2001
	• Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus • This epitope can bind three of the five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802				
p24 (121–135)	p24 (253–267)	NPPIPVGEIYKRWII	HIV-1 infection	human (B8)	Gotch1990
	• High frequency of memory and effector Gag-specific CTL				
p24 (121–135)	p24 (255–274 SF2)	NPPIPVGEIYKRWII	HIV-1 infection	human (B8)	Goulder1997a, Phillips1991
	• Longitudinal study of CTL escape mutants in people with the appropriate HLA types – little variation was observed in the immunodominant B27 epitope, relative to B8 epitopes, which varied over time • [Goulder1997a] is a review of immune escape that points out that there may be a protective effect associated with B27, and that HLA-B8 individuals tend to progress more rapidly than HLA B27 patients				
p24 (121–135)	p24 (121–135)	NPPIPVGEIYKRWII	HIV-1 infection	human (B8)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
p24 (121–140)	p24 (253–272)	NPPIPVGEIYKRWIILGLNK	HIV-1 infection	human	Lieberman1995
	• HIV-specific CTL lines developed by ex vivo stimulation with peptide				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (121–140)	p24 (253–272 SF2)	NPPIPVGEIYKRWIILGLNK	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag • Two of these 12 had CTL response to this peptide • The responding subjects were HLA-A2, A3, B8, B62, and HLA-A1, B8, B18				
p24 (121–140)	p24 (253–272 SF2)	NPPIPGEIKRWIILGNIK	HIV-1 infection	human	Lieberman1997b
	• CTL expanded ex vivo were later infused into HIV-1 infected patients				
p24 (121–140)	p24 (255–274 SF2)	NPPIPVGEIYKRWIILGLNK	HIV-1 infection	human	vanBaalen1993
	• Gag CTL epitope precursor frequencies were estimated and peptide mapping was performed				
p24 (121–142)	p24 (253–274 BH10)	NPPIPVGEIYKRWIILGLN-KIV	HIV-1 infection	human (B8)	Johnson1991
	• Gag CTL response studied in three individuals				
p24 (121–152)	Gag (183–214 LAI)	NPPIPVGEIYKRWIILGLN-KIVRMYSPTSILD	Vaccine	human	Gahery-Segard2000
	Vaccine *Vector/Type:* lipopeptide *HIV component:* six peptides • Anti-HIV lipopeptide vaccine consisting of six long amino acid peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial • A CD4+ T cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 9/10 reacted to this peptide • 9/12 tested mounted a CTL response to at least one of the six peptides; each of the six peptides elicited a CTL response in at least one individual – this peptide was particularly immunogenic, eliciting a CTL response in four vaccinees • All of the 12 tested had an IgG response to this peptide				
p24 (121–152)	Gag	NPPIPVGEIYKRWIILGLN-KIVRMYSPTSILD	HIV-1 infection, Vaccine	human (A*0201)	Seth2000
	Vaccine *Vector/Type:* lipopeptide *HIV component:* gag peptide • Immunization of 2/4 HIV seropositive HLA selected individuals with a 32 amino acid Gag lipopeptide that contains CTL epitopes restricted by HLA A33, B8, B27, B35, and Bw62 gave a transient increase in peptide-specific bulk CTL response, but they did not decrease plasma viral load. • Placebo and HLA mis-matched controls showed no change in CTL • The responders carried HLA Bw62 and B35 – the two HLA-matched that did not respond carried B35 and B8				
p24 (122–130)	p24	PPIPVGDIH	HIV-1 infection	human	Kaul2001c
	• This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative • The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire • This epitope was recognized in 1/22 HEPS sex worker controls, ML887				
p24 (122–130)	p24 (260–268 LAI)	PPIPVGDIY	HIV-1 or HIV-2 infection	human (B*3501)	Brander2001
	• C. Brander notes this is a B*3501 epitope				
p24 (122–130)	p24 (245–253 HIV-2)	NPVPVGNIY	HIV-1 infection	human (B*3501)	Rowland-Jones1995b

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (122–130)	p24 (245–253 HIV-2)	NPVPVGNIY	HIV-1 infection	human (B*3501)	Brander2001
	• C. Brander notes this is a B*3501 epitope				
p24 (122–130)	p24 (260–268 LAI)	PPIPVGDIY	HIV-1 or HIV-2 infection	human (B35)	Rowland-Jones1995b
	• Defined as minimal peptide by titration curve, PPIPVGEIY and HIV-2 form NPVPVGNIY are also recognized				
p24 (122–130)	p24 (260–268 LAI)	PPIPVGDIY	in vitro stimulation	human (B35)	Lalvani1997
	• A peptide-based protocol was optimized for restimulation of CTLp using optimized peptide and IL-7 concentrations – importantly this protocol does not stimulate a primary response, only secondary – peptide-specific CTLp counts could be obtained via staining with peptide-Class I tetramers • This peptide was one of the B35 presented test peptides used in control experiments showing that the assay gave no activity using lymphocytes from 21 healthy B35 seronegative donors				
p24 (122–130)	p24 (260–268 LAI)	PPIPVGDIY	HIV-1 infection	human (B35)	McMichael1994
	• Review of HIV CTL epitopes				
p24 (122–130)	p24 (subtype B)	PPIPVGEIY	HIV-1 exposed seronegative	human (B35)	Rowland-Jones1998b
	• HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes • This epitope is conserved among B and D clade viruses • The Clade A version of the epitope, PPIPVGDIY, was preferentially recognized by CTL				
p24 (122–130)		PPIPVGEIY	HIV-1 infection	human (B35)	Wilson2000a
	• Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers—high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load • All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39 • ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK • The subject with A*0201 had a moderatly strong response to SLYNTVATL • Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705 • No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL				
p24 (122–130)	p24	PPIPVGDIY		human (B35)	Rowland-Jones1999
	• CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5 • In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, and the B35 allele seems to be protective • HIV-2 version of this epitope is not conserved: NPVPVGNIY, but the CTLs are cross-reactive – one of five B35 CTL epitopes that are cross-reactive, see also [Rowland-Jones1995b]				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (122–130)	p24 (260–268)	PPIPVGDIY	HIV-1 infection	human (B35)	Oxenius2000
	• Epitope name: PPI • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable • One of two HLA B35+ among the eight study subjects recognized this epitope • Patient SC15 (HLA A1/68, B8/35, Bw4/6, Cw4/0704) was given acute and sustained therapy and recognized epitopes PPIPVGDIY and VPLRPMTY during 331 days of HAART treatment				
p24 (122–130)	p24 (122–130)	PPIPVGDIY	HIV-1 infection	human (B35)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
p24 (122–130)	p24 (254–262 SF2)	PPIPVGDIY	HIV-1 infection	human (B35)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-B35+ individuals that had a CTL response to this epitope broken down by group: 0/2 group 1, 0/2 group 2, and 1/1 group 3				
p24 (122–130)	p24 (260–268)	PPIPVGDIY	HIV-1 infection, HIV-1 exposed seronegative	human (B35)	Kaul2001a
	• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure • Among HLA-B35 women, 1/3 HEPS and 3/4 HIV-1 infected women recognized this epitope • The dominant response to this HLA allele was to this epitope in the 1/3 HEPS case and in the all 3/4 responsive HIV-1 infected women • Subject ML 857 shifted from a A*6802 DTVLEDINL and B35 (H/N)PDIVIYQY response prior to seroconversion to a B35 PPIPVGDIY and B35 VPLRPMTY response post-seroconversion				
p24 (122–130)		PPIPVGDIY	HIV-1 infection	human (B35)	Sabbaj2002b
	• Epitope name: Gag-PY9 • Among HIV+ individuals who carried HLA B35, 2/21 (10%) recognized this epitope • Among HIV+ individuals who carried HLA B*5301, 0/11 (0%) recognized this epitope				
p24 (122–130)	p24	PPIPVGEIY	HIV-1 infection, Vaccine	human (B35)	Hanke2000, Wee2002
	Vaccine *Vector/Type:* DNA prime with vaccinia MVA boost *Strain:* subtype A *HIV component:* p17, p24, polyepitope				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000]. • Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].				
p24 (124–138)	p24 (256–270 LAI)	IPVGEIYKRWIILGL	HIV-1 infection	human (B8)	Buseyne1993b
	• Clustering of Gag p24 CTL epitopes recognized in 29 HIV-infected people				
p24 (124–138)	Gag (256–270 LAI)	IPVEGEIYKRWIILGL	HIV-1 infection	human (B8)	Buseyne1993a
	• Vertical transmission of HIV ranges from 13% to 39% • Primary assays showed cytotoxic activity against at least one HIV protein was detected in 70% of infected children • Epitopes recognized in five children were mapped using synthetic peptides and secondary cultures • Two children, EM16 (CDC P2A+D2) and EM18 (CDC P2A), had a CTL response to this epitope, and it was shown to be presented by B8 in EM18				
p24 (127–135)	p24 (259–267 SF2)	GDIYKRWII	HIV-1 infection	human (B*0801)	McAdam1998
	• GDIYKRWII specific CTL clone also recognized GEIYKRWII				
p24 (127–135)	p24 (261–269)	GEIYKRWII	HIV-1 infection	human (B8)	Sutton1993
	• Predicted epitope based on B8-binding motifs, from larger peptide NPPIPVGEIYKRWII				
p24 (127–135)	p24 (259–267)	GEIYKRWII	in vitro stimulation	human (B8)	Zarling1999
	• This study compares the ability of macrophages and dendritic cells to stimulate primary responses in CD8+ lymphocytes isolated from HLA-appropriate HIV-uninfected donors using peptide-pulsed APC – the dendritic cells performed better as APC for the stimulation of primary responses • Strong CTL responses were elicited by the epitopes DRFYKTLRA and GEIYKRWII when presented by either immature or mature dendritic cells – macrophages were not able to prime a CTL response against DRFYKTLRA • A weak response to KLTPLCVSL was stimulated using macrophages as the APC • No detectable response was observed for the following previously-defined HIV epitopes: KIRLRPGGK, ILKEPVHGV, IRLRPGGK, GPKVKQWPL				
p24 (127–135)	p24 (259–267 LAI)	GEIYKRWII	HIV-1 infection	human (B8)	Klenerman1994
	• Naturally occurring variant GDIYKRWII may act as antagonist				
p24 (127–135)	p24 (259–267)	GEIYKRWII	HIV-1 infection	human (B8)	Betts2000
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes • 1/11 of the HLA A2+ was HLA A*0201, A31, B8, B51 and responded to this epitope as well as seven others				
p24 (127–135)	p24 (259–267)	GEIYKRWII	HIV-1 infection	human (B8)	Nowak1995
	• Longitudinal study of CTL response and study of immune escape – GDIYKRWII could also stimulate CTL, reactivity fluctuated				
p24 (127–135)	p24 (259–267)	GEIYKRWII	HIV-1 infection	human (B8)	McAdam1995
	• Equivalent sequence GDIYKRWII also recognized by CTL from some donors				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (127–135)	p24 (259–267)	GEIYKRWII	HIV-1 infection	human (B8)	Oxenius2000
	• Epitope name: GEI • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable • Six of the 7/8 study subjects that were HLA B8 recognized this epitope • Patient SC2 (HLA A1, B7/8, Cw0701/0702, DR4/53, DQ7) had CTL responsiveness against epitopes FLKEKGGL, GPKVKQWPL, and GEIYKRWII peptides – FLKEKGGL tetramer staining steadily declined and at day 1340 the FLKEKGGL stained cells were no longer detected and the escape mutant FLKENGGI was found in 8/10 clones • Patient SC9 (HLA A1/2, B8/13, Cw0/0701, DR2/11, DQ6/7) had a CTL response against epitopes FLKEKGGL, ILKEPVHGV, SQRRQDILDLWIYHTQGYFPDWQNY, and GEIYKRWII and all responses declined during therapy initiated at day 390 but were restored when therapy become intermittent. • Patient SC19(HLA A11/12, B8/44, Cw06/0701, DR3/7, DR52/53, DQ 2/8) had a CTL response to epitopes FLKEKGGL, GEIYKRWII, ACQGVGGPGHK, AVDLSHFLK, and FNCGGEFFY that declined during therapy initiated at day 197 • Patient SC10(HLA A1/3, B8/35, DR1/8, DQ 4/5) had sustained therapy started during acute infection and maintained an immunodominant response to FLKEKGGL and a response to GEIYKRWII through day 1088 • Patient SC12(HLA A1, B8/39, Cw0701/0702, DR2/3, DR51/52, DQ2/6) had sustained therapy started during acute infection and maintained an immunodominant response to FLKEKGGL throughout and minor responses to GEIYKRWII, DCKTILKAL, GGKKKYKLK – GEIYKRWII and GGKKKYKLK responses were stimulated by a brief period off therapy • Patient SC11(HLA A1, B8, Cw0201, DR3/11, DR52, DQ2/7) started therapy early, remained on therapy for 40 days, then reinitiated HAART at day 640 had a CTL response to FLKEKGGL, GPKVKQWPL, and GEIYKRWII throughout and received a benefit from the early limited course therapy				
p24 (127–135)	p24 (259–267 SF2)	GEIYKRWII	HIV-1 infection	human (B8)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-B8+ individuals that had a CTL response to this epitope broken down by group: 2/3 group 1, 2/3 group 2, and 2/2 group 3				
p24 (127–135)	p24	GEIYKRWII	HIV-1 infection	human (B8)	Oxenius2002b
	• Epitope name: GEI • Using previously defined epitopes [Oxenius2000, Oxenius2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI). • STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.				
p24 (127–135)	p24	GEIYKRWII	HIV-1 infection, Vaccine	human (B8)	Hanke2000, Wee2002
	Vaccine *Vector/Type:* DNA prime with vaccinia MVA boost *Strain:* subtype A *HIV component:* p17, p24, polyepitope				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000]. • Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].				
p24 (127–136)		GEIYKRWIIL	HIV-1 infection	human (B*0801)	Sabbaj2002b
	• Epitope name: Gag-GL10 • This study monitored epitope responses in HIV-1 infected minority women living in the United States • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release • Subject 00RCH87 was not on HAART, viral load 8300, CD4 count 313 • Among HIV+ individuals who carried HLA B08, 3/6 (50%) recognized this epitope				
p24 (128–135)	p24 (260–267 LAI)	EIYKRWII		human (B*0801)	Brander2001
	• C. Brander notes this is a B*0801 epitope				
p24 (128–135)	p24 (260–267 LAI)	EIYKRWII		human (B8)	Goulder1997g
	• Defined in a study of the B8 binding motif				
p24 (128–135)	p24 (SF2)	EIYKRWII	HIV-1 infection	human (B8)	Goulder2000a
	• The CTL-dominant response was focused on this epitope in a HIV+ Caucasian living in Boston – this epitope did not fall within the three most recognized peptides in the study • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK(p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa			
p24 (128–135)	p24 (C consensus)	DIYKRWII	HIV-1 infection	human (B8)	Goulder2000a
	• The CTL-dominant response was focused on this epitope in a HIV+ South African – this epitope did not fall within the five most recognized peptides in the study • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK(p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa			
p24 (128–135)	p24 (SF2)	EIYKRWII	HIV-1 infection	human (B8)	Goulder2001a
	• Epitope name: EI8 • This peptide elicited a weak CTL response during acute HIV-1 infection in patient PI004				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Three CTL responses to epitopes, TSTLQEQIGW, ISPRTLNAW, and KAFSPEVIPMF, were evident early after infection; CTL responses to SLYNTVATL, QASQEVKNW, EIYKRWII, and FLKEKGGL were detectable at 5 months post-infection and beyond				
p24 (128–135)	p24	EIYKRWII	HIV-1 infection	human (B8)	Kostense2001
	• HLA tetramers to six epitopes were used to study HLA-A2, B8 and B57 CTL in 54 patients – HIV-specific tetramer positive cells were inversely correlated with viral load in patients with high CD4, but in patients with CD4 T-cells below 400 high tetramer frequencies were found despite high viral load • Most patients have high levels of HIV-specific T-cell expansions, but many of these cells aren't functional • In 15 of the patients, the proportion of IFN gamma producing tetramer cells correlated with AIDS-free survival • 4/13 patients that reacted with EIYKRWII displayed epitope mutations in a minority of sequences, which did not correlate with disease progression or viral load – these mutations were: Patient 156 (KIYKRWMI), Patient 36 (EIYKRRII), Patient 656 (KIYKRWII, EIYERWMI), and Patient 159 (EIYKRWVI). • Stimulation with HLA-B8 p24 and Nef epitopes significantly increased Nef-specific T-cell numbers in 2 patients (748 and 1113) • There were more functional IFN-gamma producing Nef-specific T-cells within the T-cell population than there were active p24 Gag-specific T-cells			
p24 (128–135)	p24 (259–267)	DIYKRWII	HIV-1 infection	human (B8)	Appay2000
	• Combined tetramer and intracellular cytokine staining was used to study the function of circulating CD8+ T cells specific for HIV and CMV • HIV-specific CD8+ T cells expressed lower levels of perforin than CMV-specific CD8+ T cells from the same donor, and this was associated with persistent CD27 expression on HIV-specific cells, suggesting impaired maturation • In most donors, between 50% and 95% of the activated virus-specific CD8+ T cells produced IFN-γ and MIP-1β with a distinct subset that failed to produce TNF-α				
p24 (128–135)	p24 (128–135)	EIYKRWII	HIV-1 infection	human (B8)	Day2001
	• B8-restricted CTL accounted for about 1/3 of the total CTL response in one individual				
p24 (128–135)	Gag	EIYKRWII	HIV-1 infection	human (B8)	Goulder2000b
	• Tetramer assays were compared with three functional assays in 42 people with chronic HIV infection: ELISPOT, intracellular cytokine staining, and precursor frequency (limiting dilution assay [LDA]) • HIV-specific tetramer staining CTLs appeared to be active, and inert CTL were not found to play a significant role in chronic pediatric or adult HIV infection				
p24 (128–135)	p24	DIYKRWII	HIV-1 infection	human (B8)	Appay2002
	• Four HIV patients with prolonged clinically successful anti-viral therapy but with ongoing evidence of replication and Nef mRNA transcription, showed specific T-cell responses by Elispot and Tetramer staining, maintained for 2-4 years after initiation of HAART. • Nef epitope recognition was detected in all 4 subjects, gp120, Pol and Gag-specific in 1 or 2 subjects. • The HIV-specific CD8+ T-cells had an intermediate maturation phenotype characterized by low levels of perforin and high levels of CD27 expression.				
p24 (129–136)	p24 (263–270 SF2)	IYKRWIIL	HIV-1 infection	human (A*2402)	Ikeda-Moore1997
	• Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402 • This peptide induced CTL in 1/4 HIV-1+ people tested • IYKRWIIL bound to A*2402 with medium strength, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained				
p24 (129–138)	p24 (263–272 SF2)	IYKRWIILGL	HIV-1 infection	human (A*2402)	Ikeda-Moore1997
	• Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This peptide induced CTL in 1/4 HIV-1+ people tested • IYKRWIILGL bound to A*2402 with medium strength, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained				
p24 (129–138)	p24 (263–272)	IYKRWIILGL	HIV-1 infection	human (B27)	Betts2000
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes • 1/11 of the A2+ individuals was B27 and responded to IYKRWIILGL				
p24 (130–148)	p24 (265–280 BRU)	YKRWIILGLNKIVRMYSPT	HIV-1 infection	human (B27)	Dadaglio1991
	• Used as a positive control for HLA specificity				
p24 (131–139)	Gag (265–273)	KRWIILGLN	HIV-1 infection	chimpanzee (Patr-B*03)	Balla-Jhagjhoorsingh1999b
	• Certain HLA-alleles have been associated with long-term survival – among them are HLA-B*27 and HLA-B*57 • Of more than 150 chimpanzees that have been reported to be infected with HIV-1, only one has developed AIDS • CTL responses were studied in two HIV-1 infected chimpanzees that have strong CTL responses, and they were found to respond to highly conserved epitopes that are recognized in humans in the context of HLA-B*27 and HLA-B*57 • The human HLA protein which presents this Patr-B*03 epitope is HLA B*2705 but the amino acid sequences in the binding pockets of HLA-B*2705 and Patr-B*03 are distinctive				
p24 (131–140)	Gag (263–272 LAI)	KRWILLGLNK	HIV-1 infection	human	Buseyne1993a
	• Vertical transmission of HIV ranges from 13% to 39% • Primary assays showed cytotoxic activity against at least one HIV protein was detected in 70% of infected children • Epitopes recognized in five children were mapped using synthetic peptides and secondary cultures • Patient EM28 (CDC P2A) had a CTL response to four epitopes in Gag				
p24 (131–140)	p24 (263–272)	KRWIILLGLNK	HIV-1 infection	human (B*27)	Huang2000
	• The single cell ELISPOT assay was optimized and highly specific, and found to work well even after the primary cells had been frozen and thawed • Increases in gamma interferon producing cells were observed in response to anti-retroviral therapy using single cell IFN-gamma-production ELISPOT • In 3/3 HLA A*02, B*27 individuals, the dominant response in gag measured by both gamma IFN production and T cell lysis was to the B27 epitope, KRWIILLGLNK, not the A2 SLYNTVATL epitope				
p24 (131–140)	p24 (263–272 SF2)	KRWIILGLNK	HIV-1 infection	human (B*27)	McAdam1998
	• Epitope invariant across clades A, B, C, and D				
p24 (131–140)	p24 (260–269 HIV-2)	RRWIQLGLQK		human (B*2703)	Brander2001
	• C. Brander notes this is a B*2703 epitope				
p24 (131–140)	p24	KRWIILGGLNK	HIV-1 infection	human (B*2705)	Wilson2000a
	• Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load was also found • All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39 • Tetramers with peptide variants KRWIILGGLNK and KRWIIMGGLNK were used – CTL from most B27 donors recognize both variants, although one of the three subjects recognized only KRWIILGGLNK				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK • The subject with A*0201 had a moderatly strong strong response to SLYNTVATL • Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705 • No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL			
p24 (131–140)	p24 (263–272 LAI)	KRWIILGLNK	HIV-1 infection	human (B*2705)	Brander2001
	• C. Brander notes this is a B*2705 epitope				
p24 (131–140)	p24 (263–272)	KRWIILGLNK	HIV-1 infection	human (B*2705)	Kelleher2001b
	• A mutation in 4/5 B*2705 patients had substitution to lysine (K) at HIV-1 gag residue 264 (R264K), in three the change occurred late in infection – in one patient a substitution of glycine at HIV-1 gag residue 264 (R264G) was detected – these substitutions reduce binding to B27 • The R264K mutations were associated with a L268M mutation that may be compensatory, and R264G occurred in conjunction with E260D • Positions 260, 264, and 268 all lie along one aspect of helix seven of the capsid protein, a region that is important for capsid self-association and assembly • R264G and R264K escape mutation outgrowth occurred in conjunction with high viral loads				
p24 (131–140)	p24 (263–272)	KRWIIMGLNK	HIV-1 infection	human (B*2705)	Appay2000
	• Combined tetramer and intracellular cytokine staining was used to study the function of circulating CD8+ T cells specific for HIV and CMV • HIV-specific CD8+ T cells expressed lower levels of perforin than CMV-specific CD8+ T cells from the same donor, and this was associated with persistent CD27 expression on HIV-specific cells, suggesting impaired maturation • In most donors, between 50% and 95% of the activated virus-specific CD8+ T cells produced IFN-γ and MIP-1β with a distinct subset that failed to produce TNF-α				
p24 (131–140)	p24	KRWIILLGLNK	HIV-1 infection, Vaccine	human (B*2705)	Hanke2000, Wee2002
	Vaccine *Vector/Type:* DNA prime with vaccinia MVA boost *Strain:* subtype A *HIV component:* p17, p24, polyepitope • The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000]. • Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].				
p24 (131–140)	p24 (263–272 LAI)	KRWIILGLNK	HIV-1 infection	human (B*2705, B27)	Goulder1997c, Goulder1997a
	• HLA-B*2705 is associated with slow HIV disease progression • 11/11 HLA-B*2705 donors make a response to this epitope, usually an immunodominant response • This is a highly conserved epitope • The HLA-B*2705 binding motif includes R at position 2, and L in the C-term position				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• [Goulder1997a] is a review on CTL immune escape that discusses this epitope in the context of the difficulty in detection of immune escape – KRWIILGLNK and an R2K change, KKWIILGLNK, show little difference in titration curves, yet the K2 variants fail to bind to targets for more than 1 hour, while the R2 form can sensitize lysis by CTL for over 24 hours – minigene transfection experiments confirmed the importance of this for the CTL response				
p24 (131–140)	p24 (260–269 HIV-2)	RRWIQLGLQK		human (B27)	Brander1996b
	• HIV-2, HLA-B*2703, S. Rowland-Jones, Pers. Comm.				
p24 (131–140)	p24 (263–272 LAI)	KRWIILGLNK	HIV-1 infection	human (B27)	Fan1997
	• The capacity of dendritic cells to process and present antigen and stimulate anti-HIV-1 CTL memory responses was studied				
p24 (131–140)	Gag (263–272)	KRWIILGLNK	HIV-1 infection	human (B27)	Zheng1999
	• Protein delivery (gp160 LAV, p66 LAV, and p24 NY5) to human dendritic cells (DC) with liposomes provides enhanced memory CTL response relative to delivery of protein alone • Chloroquine administration enhanced epitope presentation, and brefeldin A and peptide aldehyde inhibitors inhibited antigen presentation, suggesting epitopes were processed by classical proteasome pathway • The CTL response to p24 was measured in individuals with a response to B27-KRWIILGLNK				
p24 (131–140)	p24 (263–272 LAI)	KRWIILGLNK	HIV-1 infection	human (B27)	Wilson1998a
	• HIV+ individuals were followed longitudinally using MHC tetramers in combination with 14 anti-BV chain MAbs, and clonal expansion of HIV-specific T cells was followed in vivo • Seven HIV+ people were studied, and all showed expansions of particular TCR BV clones, often several, relative to uninfected controls • Three patients were followed in detail, TCR VB expansions persisted for 2 to 3 years, with occasional transient increases				
p24 (131–140)	p24	KRWIILGLNK	HIV-1 infection	human (B27)	Rowland-Jones1997
	• Described in this review as the first identified HIV CTL epitope				
p24 (131–140)	p24 (263–272 LAI)	KRWIILGLNK	HIV-1 infection	human (B27)	Buseyne1993b
	• Clustering of Gag p24 CTL epitopes recognized in 29 HIV-infected people				
p24 (131–140)	p24 (263–272 LAI)	KRWIILGLNK	HIV-1 infection	human (B27)	McMichael1994
	• Review of HIV CTL epitopes				
p24 (131–140)	p24 (263–272)	KRWIIMGLNK	HIV-1 infection	human (B27)	Klenerman1994
	• Naturally occurring variant KRWIILGLNK may act as antagonist				
p24 (131–140)	p24 (263–272)	KRWIIMGLNK	HIV-1 infection	human (B27)	Klenerman1995
	• Naturally occurring variant KRWIILGLNK may act as antagonist				
p24 (131–140)	p24 (265–274)	KRWIILGLNK	HIV-1 infection	human (B27)	Moss1995
	• In one individual, TCR usage changed over time indicating that new populations of CTL can be recruited • TCR usage showed a CTL clonal response to this epitope that persisted over 5 years • CTL clones specific for HIV epitopes may represent between 0.2 and 1% of the total CD8+ population of T cells				
p24 (131–140)	p24 (265–276)	KRWIILGLNK		human (B27)	Carreno1992
	• Included in HLA-B27 binding peptide competition study				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (131–140)	p24 (265–274 SF2)	KRWIILGLNK	HIV-1 infection	human (B27)	Goulder1997a, Phillips1991
• Longitudinal study of CTL escape mutants – little variation was observed in the immunodominant B27 epitope, relative to B8 epitope • [Goulder1997a] is a review of immune escape that points out that there may be a protective effect associated with B27, and that HLA-B8 individuals tend to progress more rapidly than HLA B27 patients					
p24 (131–140)	p24 (263–272)	KRWIILGLNK	HIV-1 infection	human (B27)	Goulder1997a, Nietfeld1995
• Single point mutations were introduced and viral viability and CTL recognition tested – an Arg to Lys change at anchor position P2 abrogates binding to B27, but doesn't change viral viability in vitro • [Goulder1997a] is a review of immune escape that summarizes this study					
p24 (131–140)	p24 (263–272)	KRWIIMGNK	HIV-1 infection	human (B27)	Nowak1995
• Longitudinal study of CTL response and immune escape – the form KRWIILGNK was also found, and both forms stimulate CTL					
p24 (131–140)	p24 (263–272)	KRWIILGNK	HIV-1 infection	human (B27)	Durali1998
• Cross-clade CTL response was studied by determining the CTL activity in seven patients from Bangui, (6 A subtype, and 1 AG recombinant infections) and one A subtype infection from a person living in France originally from Togo, to different antigens expressed in vaccinia • Pol reactivity: 8/8 had CTL to A subtype, and 7/8 to B subtype, and HIV-2 Pol was not tested • Gag reactivity: 7/8 reacted with A or B subtype gag, 3/8 with HIV-2 Gag • Nef reactivity: 7/8 reacted with A subtype, and 5/8 with B subtype, none with HIV-2 Nef • Env reactivity: 3/8 reacted with A subtype, 1/8 with B subtype, none with HIV-2 Env • One of the patients was shown to react to this epitope: KRWIILGNK					
p24 (131–140)	p24 (263–272)	KRWIIMGLNK	HIV-1 infection	human (B27)	Goulder1997f, Goulder1997a
• Six HLA-B27 donors studied make a strong response to this epitope • In 4/6 cases, this was the immunodominant or only CTL response • Two of the cases had an epitope switch to the form KKWIIMGLNK during a period of rapid decline to AIDS, following their asymptomatic period • The arginine to lysine switch is in an anchor residue, and results in immune escape due to severely diminished binding to the B27 molecule • [Goulder1997a] is a review of immune escape that summarizes this study in the context of CTL escape to fixation					
p24 (131–140)	p24	KRWIILGLNK		human (B27)	Rowland-Jones1999
• CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5 • In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, and the B35 allele seems to be protective • HIV-2 sequence: RRWIQLGLQK – this epitope was not HIV-1 and HIV-2 cross-reactive					
p24 (131–140)	Gag (263–)	KRWILGLNK	computer prediction	(B27)	Schafer1998
• This study uses EpiMatrix for T cell epitope prediction to identify possible HLA-B27 and A-2 CTL epitopes in HIV • Based on EpiMatrix predictions, 28 peptides were synthesized and tested using T2 binding assays for potential HLA A2 or B27 binding, and 12 of these were shown to bind to the predicted HLA molecule • Two of these 12 peptides had been previously identified as CTL epitopes: HLA-B27 KRWILGLNK and HLA-A2 ILKEPVHGV • This peptide sequence is not conserved between clades, but is found in most B clade isolates					

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (131–140)	p24 (263–282)	KRWIILGLNK	HIV-1 infection	human (B27)	Bernard1998
	• This study focuses on six rare long-term survivor HIV-infected people who were infected for many years without exhibiting immune dysregulation – such immunologically normal HIV-infected (INHI) cases occur at a frequency between 0.1 and 1% in the infected population • No direct CTL were found in any of the six INHIs, but above background CTLp activity was founded in 3/6 INHIs • Epitope sequences were deduced from larger reactive peptides based on HLA binding motifs – XRXXXXXXXK is a B*2705 binding motif				
p24 (131–140)	p24 (265–274 SF2)	KRWIILGLNK	HIV-1 infection	human (B27)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-B27+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 0/0 group 2, and 1/1 group 3				
p24 (131–140)	p24 (263–272)	KRWIILGLNK	HIV-1 infection, HIV-1 exposed seronegative	human (B27)	Kaul2001a
	• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure • Subject ML 1760 had an A2 response to ILK(D/E)PVHGV prior to seroconversion, and gained responses to epitopes A2 SL(F/Y)NTVATL and B27 KRWII(L/M)GLNK post-seroconversion				
p24 (131–140)	p24 (131–140)	KRWIILGLNK	HIV-1 infection	human (B27)	Day2001
p24 (131–140)	p24 (260–299)	RRWIQLGLQK	HIV-1 infection	human (B27)	Day2001
p24 (131–140)	p24 (131–140)	KRWIILGLNK	HIV-1 infection	human (B27)	Goulder2001b
	• Epitope name: KK10 • 85% of B27+ adults have CTL that recognize this epitope, but only 2/6 children did • Responses to this dominant B27-restricted Gag epitope are present during the time of decreasing viral load in acute infection • Three children who shared B27 with their mothers did not respond to this epitope and inherited escape mutations from their mothers • A transmitted R132T anchor residue mutation abrogated binding to B27 • In the three children infected with the non-binding KK10 variants, the dominant CTL specificity was still HLA-B27-restricted, but it was directed against an epitope in p17, IRLRPGGKK, only rarely recognized in adults when KRWIILGLNK is the dominant response • Mutations in this epitope were observed in autologous clones of subjects who were B27-positive with a higher frequency than those who were B27-negative (P = 0.0005) • These mutations are being sexually transmitted in adult infections				
p24 (131–140)		KRWIILGLNK	HIV-1 infection	human (B27)	Sabbaj2002b
	• Epitope name: Gag-KK10				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Among HIV+ individuals who carried HLA B27, 2/3 (66%) recognized this epitope				
p24 (131–140)	p24 (263–272 LAI)	KRWIIMGLNK	HIV-1 infection	human (B27)	Kelleher2001a
	• Ritonavir (RTV) inhibits chymotryptic activity in the 20S proteasome in vitro, as does Saquinavir (SQV) to a lesser extent; Indinavir (IDV) does not. Thus there is concern protease inhibitors may adversely effect CTL epitope processing, but this paper indicates that processing is not inhibited at therapeutically relevant concentrations of RTV when the proteasome is functioning in an intracellular context. • RTV did not reduce antigen presentation and concentration of the two immunodominant Gag CTL epitopes (KRWIIMGLNK (B27) and SLYNTVATL (A2)). • RTV did not inhibit the processing and assembly of HLA-B35 or -A2, which are assembled with a rapid and moderate time course, respectively, or of HLA-A3, -B27 and -B39.				
p24 (131–140)	p24	KRWIILGLNK	HIV-1 infection	human (B27)	Altfeld2002
	• Epitope name: B27-KK10(p24) • Peripheral blood (PB) and lymph node (LN) CD8+ T-cell responses were compared in 15 asymptomatic HIV-1 infected patients using all known optimal CTL epitopes (http://hiv-web.lanl.gov/content/hiv-db/REVIEWS/brander2001.html) for each person's class I HLA alleles. • 60 epitope responses were detected in both PB and LN samples of the 15 patients, and an additional 8 responses were detected only in LN. The total magnitude of the response was similar in LN and PB, but the percentage of CD8+ T cells in the LN is lower so the number of HIV-specific cells per million CD8+ T-cells is higher in the LN. • 1 year post-HAART treatment in five patients studied, the magnitude of the CD8 T-cell response was decreased in both LN and PB, but more dramatically in PB, and 13/25 epitope responses in the PB became undetectable, in contrast to 5/26 in the LN. • Treatment interruption following HAART induced resulted in increased viremia accompanied by the restoration of the detection of 13 epitopes that had become undetectable in the PB, and the addition of 9 novel epitope responses. • Breakdowns of epitope responses were shown for 4 individuals. Patient C displayed the greatest response to B27-KK10(p24), and in decreasing order also responded to A24-RW8(Nef), B7-IL9(gp41), A24-RL9(gp41), A24-YL8(gp41), and B7-TM9(Nef). Patient D also displayed the greatest response to B27-KK10(p24), and also responded to A30-RY11(p17), A32-PW10(RT), A30-KY11(RT), A32-RW10(gp120), and B18-YY9(Nef).				
p24 (131–140)	Gag (263–272)	KRWIILGLNK	HIV-1 infection	human (B27)	Currier2002a
	• Cross-reactive responses were found in PBMC isolated from individuals infected with either B or CRF01_AE clade viruses, as determined by Elispot assays of target cells expressing recombinant vaccinia viruses expressing HIV-1 gag, env, nef and pol from many clades. • Subject AIHP-6 (Thai, CDF01-AE infected) recognized this epitope. This subject showed cross-subtype CTL responses to gag constructs derived from subtypes A, B, C, D, F, G, and H, and this epitope was perfectly preserved in all of these but subtype A which had the sequence KRWMILGLNK. • This subject didn't respond to a Gag CRF01 sequence which had a R->K mutation in position 2.				
p24 (131–142)	p24 (265–276)	KRWIILGLNKIV	Peptide-HLA interaction	human (B27)	Jardetzky1991
	• Epitope examined in the context of peptide binding to HLA-B27				
p24 (131–142)	p24 (263–274 LAI)	KRWIILGLNKIV	HIV-1 infection	human (B27)	Fan1997
	• The capacity of dendritic cells to process and present antigen and stimulate anti-HIV-1 CTL memory responses was studied				
p24 (131–142)	p24 (131–142)	KRWIILGLNKIV	HIV-1 infection	human (B27)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (131–145)	p24 (SF2)	KRWILGLNKIVRMY	HIV-1 infection	human	Goulder2000a
	• The CTL-dominant response was focused on this epitope in a HIV+ African American living in Boston with unknown HLA – this epitope did not fall within the three most recognized peptides in the study • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK(p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa			
p24 (131–145)	p24 (263–277 LAI)	KRWIILGLNKIVMRY	HIV-1 infection	human (A33)	Buseyne1993b
	• Clustering of Gag p24 CTL epitopes recognized in 29 HIV-infected people				
p24 (131–145)	p24 (266–277)	KRWIILGLNKIVRMY	Vaccine	human (B27)	Nixon1988
	Vaccine *Vector/Type:* vaccinia *HIV component:* Gag • Gag CTL epitope mapped with rec gag-vaccinia and synthetic peptides • This was the first HIV-1 epitope to be mapped				
p24 (131–145)	p24 (266–277 LAI)	KRWIILGLNKIVMRY	HIV-1 infection	human (B27)	Meyerhans1991
	• Longitudinal study showing persistence of epitope despite CTL activity				
p24 (131–145)	p24 (265–279)	KRWIILGLNKIVRMY	HIV-1 infection	human (B27)	Nixon1990, Rowland-Jones1999
	• HIV-1 and HIV-2 cross-reactive CTL clone, highly conserved epitope • Reviewed in Rowland-Jones99, notes that it did not appear cross-reactive with HIV-2 in Rowland-Jones98, HIV-2 form: RRWIQLGLQK				
p24 (131–146)	p24 (265–279)	KRWIILGLNKIVRMYC	HIV-1 infection	human (B27)	Bouillot1989
	• HLA-B27 restricted epitope also binds to HLA-A2 and HLA-B37 in solid phase assay				
p24 (131–150)	p24 (263–282 SF2)	KRWIILGLNKIVRMYSPTSI	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag • One of these 12 A-2 had CTL response to this peptide • The responding subject was HLA-A3, A32, B51, B62				
p24 (131–150)	p24 (265–284 SF2)	KRWIILGLNKIVRMYSPTSI	HIV-1 infection	human (Bw62?)	vanBaalen1993
	• Gag CTL epitope precursor frequencies estimated				
p24 (131–152)	p24 (263–284 BH10)	KRWIILGLNKIVRMYSPTS-ILD	HIV-1 infection	human (Bw62)	Johnson1991
	• Gag CTL response studied in three individuals				
p24 (132–145)	Gag	KWILGLNKIVRMY	HIV-1 infection	human	Weekes1999a
	• Peptide 728: Memory CTL specific for HIV-1 may contribute to oligoclonal expansions within the CD57+ CD28- CD8+ CTLp populations				
p24 (132–145)	Gag	KWILGLNKIVRMY	HIV-1 infection	human (B27)	Weekes1999b
	• Peptide 728: Almost all CD8+ T cells are CD28+ at birth, and the proportion of CD28-CD8+ cells increases with age – this study examines the contribution of CD8+CD28- cells to CTL memory pools for CTL clones specific for two persistent human viruses, CMV and HIV – clones were found to be similarly distributed the CD28 depleted cell population				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• HIV CTL responses to 3 Env and 2 Gag peptides were studied • The clonal composition of the TCR Vbeta responses were studied and was found to be highly focused, with one TCR beta-chain sequence tending to dominate the peptide-specific response – clones to this epitope were Vbeta22.1				
p24 (134–143)	p24 (subtype B)	IILGLNKIVR	HIV-1 exposed seronegative	human (A33)	Rowland-Jones1998b
	• HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes • This epitope is conserved among A, B and D clade viruses				
p24 (136–145)	p24 (268–277 LAI)	LGLNKIVRMY	HIV-1 infection	human (Bw62)	McMichael1994
	• Predicted from larger peptide • Review of HIV CTL epitopes • Also P. Johnson, Pers. Comm.				
p24 (136–146)	p24 (271–281)	LGLNKIVRMYS	HIV-1 infection	human (B62)	Lubaki1997
	• Eighty two HIV-1-specific CTL clones from 5 long-term non-progressors were isolated and analyzed for breadth of response • A sustained Gag, Env and Nef response was observed, and clones were restricted by multiple HLA epitopes, indicating a polyclonal response • A subject who was B62+ had CTL that recognized this peptide, p17 KIRLRPGGKKKYKL, and one additional unknown epitope • The two clones that recognized this epitope used two different Vβ genes, further demonstrating a polyclonal response				
p24 (136–146)	p24 (136–146)	LGLNKIVRMYS	HIV-1 infection	human (B62)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
p24 (137–145)	p24 (C consensus)	GLNKIVRMY	HIV-1 infection	human	Goulder2000a
	• The CTL-dominant response was focused on this epitope in a HIV+ South African living in Durban, HLA A2/- B5802/62 Cw4/6 – this epitope did not fall within the three most recognized peptides in the study • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK(p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa				
p24 (137–145)	p24 (272–280 LAI)	GLNKIVRMY	HIV-1 infection	human (B*1501)	Brander2001
	• C. Brander notes this is a B*1501 epitope				
p24 (137–145)	p24 (272–280 LAI)	GLNKIVRMY	HIV-1 infection	human (B62)	Goulder1997a
	• This paper is a review of CTL and immune evasion, but it presents a study of a shift from an HLA-A*0201 response to SLYNTVATL, to a B62 response to GLNKIVRMY • As long as a strong CTL response to SLYNTVATL was evident, the epitope variants SLFNTVATL or SLYNTIATL dominated the viral population – eventually the CTL response to the index peptide became undetectable, the CTL response shifted to a focus on GLNKIVRMY, and the index peptide SLYNTVATL once again established itself as the dominant form				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (137–145)	p24 (SF2)	GLNKIVRMY	HIV-1 infection	human (B62)	Goulder2000a
	• The CTL-dominant response was focused on this epitope in a HIV+ African American living in Boston – this epitope did not fall within the three most recognized peptides in the study • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK(p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa			
p24 (137–145)	p24 (267–277 SF2)	GLNKIVRMY	HIV-1 infection	human (B62)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-B62+ individuals that had a CTL response to this epitope broken down by group: 0/1 group 1, 0/1 group 2, and 1/1 group 3			
p24 (137–145)	p24 (137–145)	GLNKIVRMY	HIV-1 infection	human (B62)	Day2001
	• No immunodominant responses were detected to four B62-restricted epitopes tested				
p24 (143–150)	p24 (273–283 IIIB)	RMYSPTSI	HIV-1 infection	human (B*5201)	Brander2001
	• C. Brander notes this is a B*5201 epitope				
p24 (143–150)	p24 (273–283 IIIB)	RMYSPTSI	HIV-1 infection	human (B52)	Brander1999
	• Epitope name: SL9 • Multiple natural variations in the SL9 flanking regions of the immunodominant epitope SLYNTVATL were tested and found not to adversely affect CTL recognition or prevent epitope processing, suggesting that viral escape from the HLA-A*0201-restricted CTL response against SLYNTVATL is probably not linked to variations in the flanking regions of this epitope • The CTL response to RMYSPTSI was used as a control				
p24 (143–150)	p24 (273–283 IIIB)	RMYSPTSI	HIV-1 infection	human (B52)	Wilson1999a
	• This study describes maternal CTL responses in the context of mother-to-infant transmission • Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants • No variants of this epitope were found in a non-transmitting mother that had a CTL response to this epitope				
p24 (143–150)	p24 (143–150)	RMYSPTSI	HIV-1 infection	human (B52)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
p24 (151–170)	p24 (283–302 SF2)	LDIRQGPKEPFRDYVDRFYK	HIV-1 infection	human	McAdam1998

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (155–177)	p24 (287–309)	QGPKEPFRDYVDRFYKTLR-AEQA	Vaccine	murine	Nakamura1997
	Vaccine *Vector/Type:* peptide *HIV component:* p24				
	• Mice immunized with this synthetic peptide generated specific CTLs, a proliferative response, and antibodies				
	• The amino acids shown in the epitope field were based on the numbering provided by Nakamura et al., and may not be correct				
	• The CTL epitope was shown to be located in positions 291-300				
p24 (157–178)	p24 (290–309)	PKEPFRDYVDRFYKTLRAE-QAS	HIV-1 infection	human (B14)	Musey1997
	• Cervical and peripheral blood derived CTL clones from an HIV-infected woman recognized this epitope				
p24 (159–168)	Gag (291–300)	EPFRDYVDRF	Vaccine	murine (H-2^d)	Billaut-Mulot2001
	Vaccine *Vector/Type:* DNA with DNA boost, DNA with recombinant protein boost *Strain:* LAI *HIV component:* Gag, Tat, Nef *Adjuvant:* IL18				
	• DNA vaccinated BALB/c mice primed and boosted with the multiepitopic vaccine with IL18 showed lymphoproliferative responses 7 weeks post immunization				
	• Strong but non-lasting HIV-specific CTL responses were detected by a Cr-release assay and DNA prime/DNA boost was more effective than DNA prime protein boost				
	• Immunization with either the multiepitopic DNA or with the mixed DNA vaccine induced HIV-1 specific Th1 cytokines (IL-2 and IFN-gamma)				
	• Co-administration of IL18 increased T-cell responses but decreased anti-HIV antibody levels				
p24 (159–178)	Gag (291–310)	EPFRDYVDRFFKTLRAEQAT	HIV-1 infection	human	Novitsky2002
	• HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein.				
	• Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses.				
	• This peptide was among the 8 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
p24 (159–178)	Gag (96ZM651.8)	EPFRDYVDRFFKTLRAEQAT		human (B*44031)	Novitsky2001
	• This study is provides a survey of CTL responses and full length HIV-1 genome sequences from a C subtype infected Botswanan cohort				
	• 16 of 46 (34.8%) had CTL responses to one or more peptides within the second immunodominant region region of Gag (peptides SILDIKQGPKEPFRDYVDRF, EPFRDYVDRFFKTLRAEQAT, and FKTLRAEQATQEVKNWMTDT) with ELISPOT results median and range 500 (100 to 1,250) SFC/10^6 PBMC				
	• 3 of 6 (50%) carriers of HLA-B*44031 showed CTL responses to the peptide EPFRDYVDRFFKTLRAEQAT				
p24 (161–170)		FRDYVDRFFK	HIV-1 infection	human	Kaul2001c
	• This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative				
	• The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire				
	• This epitope was recognized in 1/22 HEPS sex worker controls, ML1732				
p24 (161–170)	p24 (subtype B, D)	FRDYVDRFYK	HIV-1 infection	human (B*1801)	Ogg1998a
	• Noted in Brander 1999, this database, to be B*1801, FRDYVDRFY				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (161–170)	p24 (subtype B, D)	FRDYVDRFYK	HIV-1 infection	human (B*1801)	Brander2001
	• C. Brander notes this is a B*1801 epitope				
p24 (161–170)	p24 (161–170)	FRDYVDRFYK	HIV-1 infection	human (B18)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
p24 (161–170)	p24 (293–302)	FRDYVDRFYK	HIV-1 infection, HIV-1 exposed seronegative	human (B18)	Kaul2001a
	• Variants FRDYVDRF(Y/F)K are specific for the B,D/A,C clades • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure • Among HLA-B18 women, 3/4 HEPS and 1/9 HIV-1 infected women recognized this epitope, likelihood ratio 5.3, p value 0.04, and HEPS women tended to respond to FRDYVDRFY/FK, while infected women tended to respond to YPLTFGWCY/F • The dominant response to this HLA allele was to this epitope for all 3/4 HEPS cases and for the single HIV-1 infected women that responded to this epitope • Four epitopes were considered to be "resistant epitopes", as they were preferentially reactive in HEPS women and so may confer resistance, and these were found in three different proteins: A2 ILK(D/E)PVHGV in RT, A*6802 DTVLEDINL in Protease, B14 DLNM/TLN(I/V)V in p24 and B18 FRDYVDRF(Y/F)K also in p24 • Differences in epitope specificity were only seen for responses restricted by class I HLA alleles A2, A24, A*6802, B14, and B18, previously shown to be associated with resistance to HIV-1 in this cohort				
p24 (161–170)	p24	FRDYVDRFYK	HIV-1 infection, Vaccine	human, macaque (B18)	Hanke2000, Wee2002
	Vaccine *Vector/Type:* DNA prime with vaccinia MVA boost *Strain:* subtype A *HIV component:* p17, p24, polyepitope • The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000]. • Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].				
p24 (161–180)	p24 (293–312 SF2)	FRDYVDRFYKTLRAEQASQD	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag • One of these 12 had CTL response to this peptide • The responding subject was HLA-A2, A3, B8, B62				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (161–180)	p24 (293–312 SF2)	FRDYVDRFYKTLRAEQASQD	HIV-1 infection	human	Lieberman1997b
	• CTL expanded ex vivo were later infused into HIV-1 infected patients				
p24 (161–180)	p24 (293–312 SF2)	FRDYVDRFYKTLRAEQASQD	HIV-1 infection	human (B71)	McAdam1998
p24 (162–172)	p24 (296–306 subtype A)	RDYVDRFFKTL	HIV-1 infection	human (A*2402)	Dorrell1999
	• CTL responses in three individuals with non-clade B infections were studied, 2 with subtype A infections, 1 with subtype C – their infections all originated in East Africa • This epitope is similar to the A24 DYVDRYFKT epitope found for B subtype, but CTL from this A subtype infection required the additional Arg – the B clade sequence change from F to Y diminished CTL reactivity • C. Brander notes that this is an A*2402 epitope in the 1999 database				
p24 (162–172)	p24 (296–306 subtype A)	RDYVDRFFKTL	HIV-1 infection	human (A*2402)	Brander2001
	• C. Brander notes this is an A*2402 epitope				
p24 (162–172)	p24 (296–306)	RDYVDRFFKTL	HIV-1 infection, HIV-1 exposed seronegative	human (A24)	Kaul2001a
	• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure • Among HLA-A24 women, 0/4 HEPS and 6/10 HIV-1 infected women recognized this epitope, likelihood ratio 7.2, p value 0.03, and (R)YL(R/K)DQQLL tended to be reactive in HEPS and infected women, RDYVDRFFKTL in infected women only • The dominant response to this HLA allele was to this epitope in all of the 6/10 HIV-1 infected women • Differences in epitope specificity were only seen for responses restricted by class I HLA alleles A2, A24, A*6802, B14, and B18, previously shown to be associated with resistance to HIV-1 in this cohort • Subject ML 1707 started with a CTL response to A*6802 DTVLEDINL prior to seroconversion, and switched to A*6802 ETAYFILKL and A24 RDYVDRFFKTL post-seroconversion				
p24 (162–172)	p24 (293–312 LAI)	RDYVDRFYKTL	HIV-1 infection	human (B*4402)	Brander2001
	• C. Brander notes this is a B*4402 epitope				
p24 (162–172)	p24 (162–172)	RDYVDRFYKTL	HIV-1 infection	human (B44)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
p24 (162–172)	p24 (162–172)	RDYVDRFYKTL	HIV-1 infection	human (B44)	Day2001
p24 (162–172)	p24	RDYVDRFYKTL	HIV-1 infection, Vaccine	human, macaque (B44)	Hanke2000, Wee2002
	Vaccine *Vector/Type:* DNA prime with vaccinia MVA boost *Strain:* subtype A *HIV component:* p17, p24, polyepitope				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000]. • Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].				
p24 (162–172)	p24 (293–312 LAI)	RDYVDRFYKTL	HIV-1 infection	human (B44, A26 or B70)	Ogg1998a
p24 (163–172)	p24 (163–172)	DYVDRFYKTL	HIV-1 infection	human (A24)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
p24 (164–172)	Gag (296–304)	YVDRFYKTL	HIV-1 infection	human (A*0207)	Currier2002a
	• Cross-reactive responses were found in PBMC isolated from individuals infected with either B or CRF01_AE clade viruses, as determined by Elispot assays of target cells expressing recombinant vaccinia viruses expressing HIV-1 gag, env, nef and pol from many clades. • The Thai subject VAIP-4 demonstrated broad CTL cross-reactivity towards gag constructs derived from subtypes A, B, C, D, F, G, H, and CRF-01_AE. Sequence alignments of this epitope showed conservation for clades B and D, and Y->F substitutions at position 6 for subtypes A, C, CDR01-AE, F, G, and H. YVDRFYKTL and the variant epitope YVDRFFKTL are recognized equally well.				
p24 (164–172)	p24 (298–306 subtype A)	YVDRFFKTL	HIV-1 infection	human (A26 or B70)	Dorrell1999
	• CTL responses in three individuals with non-clade B infections were studied, 2 with subtype A infections, 1 with subtype C – their infections all originated in East Africa • This CTL epitope is conserved in A and C subtype, and B clade sequences tend to have a change from F to Y, YVDRFYKTL – both variants showed strong CTL reactivity • CTL reacted with targets presenting either in the context A26 or B70 – the epitope has the HLA-26 motif of Val at position 2 and Leu at the carboxy terminus, and the B70 anchor residue motif is unknown				
p24 (164–172)	Gag (298–306 subtype A)	YVDRFFKTL	HIV-1 infection, in vitro stimulation	human (A26 or B70)	Dorrell2001
	• In vitro restimulation of CTL specific for dominant epitopes from infected individuals is possible using recombinant modified vaccinia virus Ankara (MVA) carrying A or D subtype HIV-1 Gag proteins				
p24 (164–172)	Gag (296–304 96ZM651.8)	YVDRFFKRL		human (B*1510, B70)	Novitsky2001
	• This study provides a survey of CTL responses and full length HIV-1 genome sequences from a C subtype infected Botswanan cohort. • 4 subjects who responsed to the CTL epitope YVDRFFKTL – all were HLA-B*1510 and also shared HLA-Cw03, suggesting linkage disequilibrium • An HIV-1 B variant of the epitope YVDRFYKTL has been described, and was recognized byCTL from an HIV-1 subtype A-infected patient, and the HLA restriction of the epitope was suggested to be A26 or B70 – HLA-B*1510 is equivalent to the serological specificity HLA B70				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (164–172)	p24 (164–172)	YVDRFYKTL	HIV-1 infection	human (B70)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
p24 (166–174)	p24 (298–306 LAI)	DRFYKTLRA	HIV-1 infection	human (B*1402)	Brander2001
	• C. Brander notes this is a B*1402 epitope				
p24 (166–174)	p24 (298–306 IIIB)	DRFYKTLRA	HIV-1 infection	human (B14)	Wilson1996
	• Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study • DRFYKILRA, a naturally occurring variant, was found in mother, and is recognized although less reactive • DQFYKTLRA, a naturally occurring variant, was found in infant and is not recognized				
p24 (166–174)	p24 (298–306 IIIB)	DRFYKTLRA	HIV-1 infection	human (B14)	Cao1997a
	• The consensus peptide for clades B and D is DRFYKTLRA • The consensus peptide for clades A and C is DRFFKTLRA and it is equally reactive				
p24 (166–174)	p24 (298–306 HXB2)	DRFYKTLRA	HIV-1 infection	human (B14)	Yang1997b
	• A chimeric universal T cell receptor was created by linking CD4 or an HIV-specific anti-gp41 Ig sequence to the signaling domain of the T cell receptor chain ζ, and transducing into CD8+ cells • The response using universal-receptor-bearing CD8+ cells to lyse infected cells in vitro was comparable to the natural occurring responses of CTL-clones from HIV+ individuals in terms of kinetics and efficiency • A CTL clone specific for this epitope was used for the comparison				
p24 (166–174)	p24	DRFWKTLRA	HIV-1 exposed seronegative	human (B14)	Rowland-Jones1998a
	• A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating • The D subtype consensus is identical to the B clade epitope • The A subtype consensus is drFfKtLRA				
p24 (166–174)	p24 (298–306 LAI)	DRFYKTLRA	HIV-1 infection	human (B14)	Harrer1996b
p24 (166–174)	p24 (298–306)	DRFYKTLRA	HIV-1 infection	human (B14)	Yang1996
	• CD4+ cell lines acutely infected with HIV were studied to determine their susceptibility to lysis by CTL • Clones specific for RT lysed HIV-1 infected cells at lower levels than Env or Gag specific clones • The distinction was thought to be due to lower expression of RT relative to Env and Gag • CTL can lyse infected cells early after infection, possibly prior to viral production				
p24 (166–174)	p24 (298–306)	DRFYKTLRA	HIV-1 infection	human (B14)	Yang1997a
	• CTL inhibit HIV-1 replication at effector cell concentrations comparable to those found in vivo • CTL produced HIV-1-suppressive soluble factors – MIP-1α, MIP-1β, RANTES, after antigen-specific activation • CTL suppress HIV replication more efficiently in HLA-matched cells				
p24 (166–174)	p24 (298–306)	DRFYKTLRA	in vitro stimulation	human (B14)	Zarling1999
	• This study compares the ability of macrophages and dendritic cells to stimulate primary responses in CD8+ lymphocytes isolated from HLA-appropriate HIV-uninfected donors using peptide-pulsed APC – the dendritic cells performed better as APC for the stimulation of primary responses				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Strong CTL responses were elicited by the epitopes DRFYKTLRA and GEIYKRWII when presented by either immature or mature dendritic cells – macrophages were not able to prime a CTL response against DRFYKTLRA • A weak response to KLTPLCVSL was stimulated using macrophages as the APC • No detectable response was observed for the following previously-defined HIV epitopes: KIRLRPGGK, ILKEPVHGV, IRLRPGGK, GPKVKQWPL				
p24 (166–174)	p24	DRFYKLTRA		human (B14)	Rowland-Jones1999
	• CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5 • In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, and the B35 allele seems to be protective • HIV-2 sequence: DRFYKSLRA is cross-reactive, [Harrer1993]				
p24 (166–174)	p24 (298–306 IIIB)	DRFYKTLRA	HIV-1 infection	human (B14)	Wilson1999a
	• This study describes maternal CTL responses in the context of mother-to-infant transmission • Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants • DRFYKILRA and DQFYKTLRA were escape mutants				
p24 (166–174)	p24 (SF2)	DRFYKTLRA	HIV-1 infection	human (B14)	Goulder2000a
	• The CTL-dominant response was focused on this epitope in 2/5 HIV+ individuals who were HLA B14 living in Boston – this epitope did not fall within the three most recognized peptides in the study • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK(p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa				
p24 (166–174)	p24 (SF2)	DRFYKTLRA	HIV-1 infection	human (B14)	Goulder2001a
	• Epitope name: DA9 • Data from patient AC13 suggest a role for this epitope in initial control of viremia in acute infection, as it is one of several subdominant CTL epitopes recognized during the initial decline in viremia • A CTL response to SL9, SLYNTVATL, was not evident until 18 months post-presentation				
p24 (166–174)	p24 (166–174)	DRFYKTLRA	HIV-1 infection	human (B14)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
p24 (166–174)	p24 (298–306 SF2)	DRFYKTLRA	HIV-1 infection	human (B14)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Number of HLA-B14+ individuals that had a CTL response to this epitope broken down by group: 3/3 group 1, 1/2 group 2, and 0/0 group 3				
p24 (166–174)	p24 (298–306)	DRFFKTLRA	HIV-1 infection, HIV-1 exposed seronegative	human (B14)	Kaul2001a
	• Variants DRF(F/W)KTLRA are specific for clades A/B • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure • Among HLA-B14 women, 0/4 HEPS and 6/7 HIV-1 infected women recognized this epitope, likelihood ratio 14.4, p value 0.004 and HEPS women tended to respond to DLNMMLNIV/DLNTMLNVV, while infected women tended to respond to DRF(F/W)KTLRA • The dominant response to this HLA allele was to this epitope for all of the 6/7 HIV-1 infected women • Differences in epitope specificity were only seen for responses restricted by class I HLA alleles A2, A24, A*6802, B14, and B18, previously shown to be associated with resistance to HIV-1 in this cohort			
p24 (166–174)	p24 (SF2)	DRFYKTLRA	HIV-1 infection	human (B14)	Altfeld2000b
	• This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual				
p24 (166–174)	p24	DRFYKTLRA	HIV-1 infection	human (B14)	Cao2002
	• AC13 is a B14 restricted CTL clone that recognizes DRFYKTLRA. • CTL could be activated by a fusion protein of an HIV protein and anthrax lethal factor (LFn-HIV) that promotes antigen presenting cell uptake of exogenous protein and allows processing through the MHC class I pathway. This strategy for CTL detection could allow antigen presentation without generation of cells by the standard methods of using live viral vectors carrying a protein, or by loading the cells with peptides and by-passing processing.				
p24 (166–174)	p24	DRFWKTLRA	HIV-1 infection	human (B14)	Kaul2002
	• Neisseria gonorrhea cervititis in 9 HIV+ Kenyan sex workers caused a functional deficiency in IFN-gamma production in HIV-1 epitope-specific CD8+ T-cells, detected by intracellular cytokine production and tetramer assays, while not affecting the total number of epitope-specific CTLs. • Ghonorrhea caused the weaker HIV-1 specific CTL responses in 4 HIV-1 exposed persistently seronegative (HEPS) women to become undetectable by Elispot and tetramer assays, and CMV-specific CTL in 2 HEPS subjects were shown to have impaired function with regard to IFN-gamma production.				
p24 (166–174)	p24	DRFYKTLRA	HIV-1 infection, Vaccine	human (B14)	Hanke2000, Wee2002
	Vaccine *Vector/Type:* DNA prime with vaccinia MVA boost *Strain:* subtype A *HIV component:* p17, p24, polyepitope • The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000]. • Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (166–174)	p24 (subtype B)	DRFYKTLRA	HIV-1 exposed seronegative	human (B14, B*1402)	Rowland-Jones1998b
• HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes • This epitope is conserved among B and D clade viruses • The Clade A version of the epitope, DRFFKLTRA, was preferentially recognized by CTL • This epitope was recognized by two different exposed and uninfected prostitutes					
p24 (166–175)	p24 (298–306 HX10)	DRFYKTLRAE	HIV-1 infection	human (B14)	Wagner1999
• The immunodominant CTL response in a long-term survivor was to this highly conserved and functionally relevant epitope • By testing mutations in an HXB2 background, it was found that all mutations within the epitope that abrogated CTL recognition also abolished viral infectivity • The epitope in this study overlaps the major homology region for which highly conserved residues exist in all known lenti- and onco-viruses and yeast transposons • Patient was part of the study in [Harrer1996a]					
p24 (169–188)	Gag (301–320)	FKTLRAEQATQDVKNWMTDT	HIV-1 infection	human	Novitsky2002
• HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 8 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.					
p24 (173–181)		RAEQASQEV	HIV-1 infection	human	Kaul2001c
• This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative • The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire • This epitope was 1/22 HEPS sex worker controls ML1792					
p24 (173–181)	p24 (305–313)	RAEQASQEV	HIV-1 infection	human (Cw8)	Johnson1991
• Originally reported as HLA-B14 restricted, but subsequently found not to be presented by cells transfected with B14 • Thought to be HLA-Cw8 restricted (C. Brander and B. Walker)					
p24 (173–181)	p24	RAEQASQEV	HIV-1 exposed seronegative	human (Cw8)	Rowland-Jones1998a
• A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating • The A subtype consensus is RAeQAtQEV • The D subtype consensus is RAEQsQdV • Thought to be HLA-Cw8 restricted, not B14 as originally reported (C. Brander, B. Walker, and S. Rowland-Jones, personal communication)					
p24 (173–181)	p24 (305–313)	RAEQASQEV	HIV-1 infection	human (Cw8)	Price1995
• Study of cytokines released by HIV-1 specific activated CTL • Thought to be HLA-Cw8 restricted, not B14 as originally reported (C. Brander, B. Walker, and S. Rowland-Jones, personal communication)					

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (173–181)	p24 (305–313)	RAEQASQEV	HIV-1 infection	human (Cw8)	Lubaki1997
	• Eighty two HIV-1-specific CTL clones from 5 long-term non-progressors were isolated and analyzed for breadth of response • A sustained Gag, Env and Nef response was observed, and clones were restricted by multiple HLA epitopes, indicating a polyclonal response • Despite this being a well defined conserved epitope, and thought to be presented by B14, none of the 11 gag-specific clones from a B-14 positive subject could recognize either it or p24 PQDLNTMLN • Thought to be HLA-Cw8 restricted, not B14 as originally reported (C. Brander, B. Walker, and S. Rowland-Jones, personal communication)				
p24 (173–181)	p24 (305–313)	RAEQASQEV	HIV-1 infection, HIV-1 exposed seronegative	human (Cw8)	Kaul2001a
	• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers				
p24 (174–184)	p24 (306–316 LAI)	AEQASQDVKNW		human (B*4402)	Brander2001
	• C. Brander notes this is a B*4402 epitope				
p24 (174–184)	p24 (306–316 LAI)	AEQASQDVKNW		human (B*4402, B44)	Brander1997
	• Pers. Comm. from D. Lewinsohn to C. Brander and B. Walker, C Brander et al., this database, 1999				
p24 (174–184)	Gag (306–316)	AEQASQEVKNW	HIV-1 infection	human (B44)	Brodie1999
	• The ability of CTL effector cells was studied by expanding autologous HIV-1 Gag-specific CTL in vitro, and adoptively transferring them • The transferred CTLs migrated to the lymph nodes and transiently reduced circulating productively infected CD4+ T cells, showing that CTL move to appropriate target sites and mediate anti-viral effects				
p24 (174–184)	p24 (306–316)	AEQASQEVKNW	HIV-1 infection	human (B44)	Brodie2000
	• Study tracks and quantifies *in vivo* migration of neo-marked CD8 HIV-specific CTL • Adoptively transferred gene-marked HIV-specific CTL homed to specific lymph node sites, colocalizing within the parafollicular regions of the lymph node adjacent to cells expressing HIV tat-fusion transcripts, indicative of viral replication • The CTL clones expressed CCR5 and localized among HIV-1 infected cells expressing MIP-1alpha and MIP-1beta, CC-chemokines produced at sites of viral replication, suggesting a possible homing mechanism • This study provides a methodology for tracking and studying antigen specific CTL *in vivo*				
p24 (174–184)	p24 (306–316 LAI)	AEQASQDVKNW	HIV-1 infection	human (B44)	Mollet2000
	• Epitope name: G3 • A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses • In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished • Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change				
p24 (174–184)	p24 (174–184)	AEQASQDVKNW	HIV-1 infection	human (B44)	Day2001
	• B44-restricted CTL response was strongest to this epitope in one individual				
p24 (174–184)	p24	AEQASQDVKNW	HIV-1 infection	human (B44)	Altfeld2002
	• Epitope name: B44-AW11(p24)				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Peripheral blood (PB) and lymph node (LN) CD8+ T-cell responses were compared in 15 asymptomatic HIV-1 infected patients using all known optimal CTL epitopes (http://hiv-web.lanl.gov/content/hiv-db/REVIEWS/brander2001.html) for each person's class I HLA alleles. • 60 epitope responses were detected in both PB and LN samples of the 15 patients, and an additional 8 responses were detected only in LN. The total magnitude of the response was similar in LN and PB, but the percentage of CD8+ T cells in the LN is lower so the number of HIV-specific cells per million CD8+ T-cells is higher in the LN. • 1 year post-HAART treatment in five patients studied, the magnitude of the CD8 T-cell response was decreased in both LN and PB, but more dramatically in PB, and 13/25 epitope responses in the PB became undetectable, in contrast to 5/26 in the LN. • Treatment interruption following HAART induced resulted in increased viremia accompanied by the restoration of the detection of 13 epitopes that had become undetectable in the PB, and the addition of 9 novel epitope responses. • Breakdowns of epitope responses were shown for 4 individuals. Patient B displayed the greatest response to epitope B44-AW11(p24) and also responded to A32-PW10(RT) in both PB and LN samples, while a third response against epitope A32-RW10(gp120) was only detected in the LN sample.				
p24 (175–186)	p24 (307–318)	EQASQEVKNWMT	HIV-1 infection	human (B44)	Quayle1998
	• HIV is found in semen both as cell-associated and cell-free forms, and HIV-specific CTL could be found in the semen of 5/5 men with CD4 greater than 500 – 3 of the men were analyzed in detail and had broad CTL to gag, env and pol • Two CTL lines from one donor recognized this epitope • Isolation of CTLs specific to HIV in both male and female urinal tracts provide evidence that virus-specific lymphocytes come from the urogenital mucosa, and the authors speculate that CTL in mucosal tissues may be correlated with lower viral load in semen and reduced transmission				
p24 (176–184)	p24 (308–316 LAI)	QASQEVKNW	HIV-1 infection	human (B*5301)	Brander2001
	• C. Brander notes this is a B*5301 epitope				
p24 (176–184)		QASQEVKNW	HIV-1 infection	human (B*5301, B57)	Sabbaj2002b
	• Epitope name: Gag-QW9 • This study monitored epitope responses in HIV-1 infected minority women living in the United States • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release • Subject 01RCH59 was Hispanic, was not on HAART, viral load 5100, CD4 count 349, and she also recognized PIQKETWETW, RT(392-401), A*3201 • Among HIV+ individuals who carried HLA B*5301, 11/15 (73%) recognized this epitope • Among HIV+ individuals who carried HLA B57, 3/6 (60%) recognized this epitope				
p24 (176–184)	p24 (309–317 LAI)	QASQEVKNW	HIV-1 infection	human (B*5701)	Goulder1996b
	• Recognition of this peptide by two long-term non-progressors • Peptide defined on the basis of B*5801 binding motif, yet not cross-restricted except at high concentrations • Described as B*5701 in C. Brander et al., this database, 1999				
p24 (176–184)	p24 (311–319 LAI)	QASQEVKNW	HIV-1 infection	human (B*5701)	Brander2001
	• C. Brander notes this is a B*5701 epitope				
p24 (176–184)		QASQEVKNW	HIV-1 infection	human (B*5701)	Migueles2001
	• HLA B*5701 was found in a very high frequency in HIV-1 infected non-progressors, 11/13 (85%) versus 19/200 (9.5%) of progressors. Non-progressors tended to have an immune response that was highly focused on four p24 epitopes that were presented by B*5701, ISPRTLNAW, KAFSPEVIPMF, TSTLQEQIGW, and QASQEVKNW. • Only QASQEVKNW was recognized in all of the LTNP's tested.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (176–184)		QASQEVKNW	HIV-1 infection	human (B*5701)	Migueles2001
• CTL activity was monitored in 27 individuals, including 10 LTNP with an over-expression of HLA B*5701 – these individuals have viral loads below the threshold of infection without therapy, and their CD8+ T-cell response tends to be focused on peptides that contain B*5701 epitopes ISPRTLNAW, KAFSPEVIPMF, TSTLQEQIGW, or QASQEVKNW. • CTL responses are broader in B*5701+ individuals with progressive viremia than those that control viremia. • The HLA-A*0201 SLYNTVATL epitope response was not as strong individuals that carried both A2, B57.					
p24 (176–184)	p24 (308–316 LAI)	QASQEVKNW	HIV-1 infection	human (B53)	Buseyne1997
• Minimal sequence determined through epitope mapping • This is a relatively conserved epitope • HLA-Cw*0401 was defined as the restricting element, but cells that carry Cw*0401 varied in their ability to present this epitope – this could be the result of diminished cell-surface expression of Cw*0401 in some cells • The HLA presenting molecule for this epitope was originally described as Cw*0401, but subsequent experiments with an HLA B53+ C4- cell line and with C1R cells transfected with HLA-B53 have shown that the HLA restricting element is HLA-B53 (Pers. Comm., Dr. Florence Buseyne, 2000)					
p24 (176–184)	(LAI)	QASQEVKNW		human (B53)	Brander2001, Buseyne1999
p24 (176–184)	p24 (NL43)	QASQEVKNW	in vitro stimulation	human (B53)	Buseyne2001
• Epitope name: QW9 • Exogenous presentation or cross-presentation of epitopes by antigen presenting cells (APC) without protein synthesis is an alternative pathway for CTL epitope processing that may be important in the initial generation of viral specific CTL • Dendritic cells treated with AZT to inhibit protein synthesis were able to elicit a strong specific CTL response in QASQEVKNW specific CTL clone 141 without protein synthesis, while macrophages demonstrated a decreased presentation efficiency • Exogenous Gag epitope presentation was Env-dependent and required receptor-dependent fusion					
p24 (176–184)	p24 (308–316)	QATQEVKNW	HIV-1 infection, HIV-1 exposed seronegative	human (B53)	Kaul2001a
• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure • Among HLA-B53 women, 1/2 HEPS and 7/9 HIV-1 infected women recognized this epitope					
p24 (176–184)	p24 (308–316 subtype A consensus)	QATQEVKNM	HIV-1 infection	human (B53)	Dorrell2001
• In clade A infected Gambians, three HLA-B53 epitopes were defined in Gag p24 using ELISPOT, tetramer, and cytotoxicity assays • Two of the new epitopes lacked the predicted by P2 anchors, DTINEEAAEW and QATQEVKNM, and bound to B53 with high affinity, thus extending the anchor residue motif for B53 and the related B35 • While S, T, and P could all fit into the HLA-B35 or HLA-B53 B pocket and form a hydrogen bond, A would not form a bond, so the authors propose compensatory interactions account for the high affinity of QATQEVKNM for B53 • QATQEVKNM was recognized in 6/7 HLA-B53 subjects					

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Cross-recognition of QATQEVKNM was not studied here, but it was noted that both the A, QATQEVKNM, and B, QASQDVKNW, subtype version of this epitope, are also presented by HLA-B57 and B58, common HLA alleles in Africans				
p24 (176–184)	Gag (SF2) • Epitope name: QW9 • This peptide elicited a weak CTL response during acute infection of patient PI004 • Three CTL responses, to epitopes TSTLQEQIGW, ISPRTLNAW, and KAFSPEVIPMF, were evident early after infection; CTL responses to SLYNTVATL, QASQEVKNW, EIYKRWII, and FLKEKGGL were detectable at 5 months post-infection and beyond	QASQEVKNW	HIV-1 infection	human (B57)	Goulder2001a
p24 (176–184)	(LAI)	QASQEVKNW		human (Cw4)	Brander2001, Buseyne1999
p24 (176–184)	p24 (176–184) • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers	QASGEVKNW	HIV-1 infection, HIV-1 exposed seronegative	human (Cw4)	Kaul2001a
p24 (176–185)	p24 (311–319 SF2) • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-B57+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 0/0 group 2, and 1/2 group 3	QASKEVKNWV	HIV-1 infection	human (B57)	Altfeld2001b
p24 (177–185)	p24 (177–185) • Variants A(T/S)QEVKNWM are specific for the A/B clades • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure • Among HLA-B53 women, 1/2 HEPS and 5/9 HIV-1 infected women recognized this epitope • The dominant response to this HLA allele was to this epitope in the 1/2 HEPS case and in only one of the 5/9 HIV-1 infected women	ATQEVKNWM	HIV-1 infection, HIV-1 exposed seronegative	human (B53)	Kaul2001a
p24 (180–189)	p24 (313–322) • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers	EVKNWMTETL	HIV-1 infection, HIV-1 exposed seronegative	human (B53)	Kaul2001a
p24 (181–190)	p24 (313–322 LAI) • P. Johnson, pers. comm.	VKNWMTETLL		human (B8)	Brander1996b

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (191–205)	Gag (320–328 BH10, LAI)	VQNANPDCKTILKAL	HIV-1 infection	human	Maksiutov2002
	• This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins. • This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is TLLVQNANP) has similarity with growth differentiation factor 11, fragment THLVQQANP.				
p24 (191–205)	p24 (191–205)	VQNANPDCKTILKAL	HIV-1 infection	human (B51)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
p24 (191–205)	p24 (323–337)	VQNANPDCKTILKAL	HIV-1 infection	human (B8)	Nixon1991
	• Two CTL epitopes defined (see also p17(21-35))				
p24 (191–205)	p24 (325–339 SF2)	VQNANPDCKTILKAL	HIV-1 infection	human (B8)	Goulder1997a, Phillips1991
	• Longitudinal study of CTL escape mutants in people with the appropriate HLA types – little variation was observed in the immunodominant B27 epitope, relative to the B8 epitopes, which varied over time • [Goulder1997a] is a review of immune escape that points out that there may be a protective effect associated with B27, and that HLA-B8 individuals tend to progress more rapidly than HLA B27 patients				
p24 (191–210)	p24 (323–342 SF2)	VQNANPDCKTILKALGPAAT	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag • Three of these 12 had CTL response to this peptide • The responding subjects were HLA-A3, A24, B8, B55; HLA-A1, A11, B8, B27				
p24 (191–210)	p24 (323–342 SF2)	VQNANPDCKTILKALGPAAT	HIV-1 infection	human	Lieberman1997b
	• CTL expanded ex vivo were later infused into HIV-1 infected patients				
p24 (193–201)	Gag (327–335 SF2)	NANPDCKTI	HIV-1 infection	human (B*5101)	Tomiyama1999
	• HLA-B27, -B51, and -B57 are associated with slow progression to AIDS, while HLA-B35, -B8, -B24 are associated with a rapid progression to AIDS (Nat. Med. 2:405, 1996;Lancet 22:1187, 1986;Hum Immunol 22:73, 1988;Hum Immunol 44:156, 1995) • 15% of Japanese populations carry HLA-B51 while HLA-B27 and -B57 are detected in less than 0.3% • Of the 172 HIV-1 peptides with HLA-B*5101 anchor residues, 33 bound to HLA-B*5101, seven of these peptides were reactive with CTL from 3 B*5101 positive individuals, and six were properly processed • Four of the six epitopes were highly conserved among B subtype sequences, NANPDCKTI is conserved				
p24 (193–201)	p24 (325–333)	NANPDCKTI?	HIV-1 infection	human (B51)	Betts2000
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes • 3/11 of the HLA A2+ individuals were HLA B51 and two of these responded to this epitope as well as to other epitopes				
p24 (193–201)	p24 (324–335 IIIB)	NANPDCKTI	HIV-1 infection	human (B51)	Wilson1999a
	• This study describes maternal CTL responses in the context of mother-to-infant transmission • Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• No variants of this epitope were found in a non-transmitting mother that had a CTL response to this epitope				
p24 (193–201)	p24 (323–333)	NANPDCKTI	HIV-1 infection	human (B51)	Oxenius2000
	• Epitope name: NAN • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable • None of the 8 study subjects recognized this epitope but none were HLA B51+				
p24 (193–201)	p24 (191–205)	NANPDCKTI	HIV-1 infection	human (B8)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
p24 (195–202)	p24 (323–342)	NPDCKTIL	HIV-1 infection	human (B35)	Bernard1998
	• This study focuses on six rare long-term survivor HIV-infected people who were infected for many years without exhibiting immune dysregulation – such immunologically normal HIV-infected (INHI) cases occur at a frequency between 0.1 and 1% in the infected population • No direct CTL were found in any of the six INHIs, but above background CTLp activity was founded in 3/6 INHIs • Epitope sequences were deduced from larger reactive peptides based on HLA binding motifs – XPXXXXXL is a B35 binding motif				
p24 (195–202)		NPDCKTIL	HIV-1 infection	human (B35)	Sabbaj2002b
	• Epitope name: Gag-NL8 • Among HIV+ individuals who carried HLA B35, 3/17 (18%) recognized this epitope				
p24 (197–205)	p24 (329–337 LAI)	DCKTILKAL		human (B*0801)	Brander2001
	• C. Brander notes this is a B*0801 epitope				
p24 (197–205)	p24 (329–337 LAI)	DCKTILKAL		human (B8)	Sutton1993
	• Predicted epitope based on B8-binding motifs, from larger peptide VQNANPDCKTILKAL				
p24 (197–205)	p24 (329–337)	DCKTILKAL	HIV-1 infection	human (B8)	Nowak1995
	• In a longitudinal study of CTL response and immune escape – the variant DCRTILKAL was also found, binds to B8, but is not recognized				
p24 (197–205)	p24 (329–337)	DCKTILKAL		human (B8)	McAdam1995
	• Defined as minimal epitope by titration and binding studies				
p24 (197–205)	p24 (197–205)	DCKTILKAL		human (B8)	Goulder1997g
	• Included in a study of the B8 binding motif				
p24 (197–205)	p24 (329–337)	DCKTILKAL	HIV-1 infection	human (B8)	Oxenius2000
	• Epitope name: DCK • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable • This epitope was recognized at a low level by only 1 of the 7/8 study subjects that were HLA B8				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Patient SC12(HLA A1, B8/39, Cw0701/0702, DR2/3, DR51/52, DQ2/6) had sustained therapy started during acute infection and maintained an immunodominant response to FLKEKGGL throughout and minor responses to GEIYKRWII, DCKTILKAL, GGKKKYKLK – GEIYKRWII and GGKKKYKLK responses were stimulated by a brief period off therapy				
p24 (197–205)	p24 (197–205)	DCKTILKAL	HIV-1 infection	human (B8)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
p24 (197–205)	p24 (197–205)	DCKTILKAL	HIV-1 infection	human (B8)	Day2001
	• B8-restricted CTL accounted for about 1/3 of the total CTL response in one individual				
p24 (197–205)	p24	DCKTILKAL	HIV-1 infection	human (B8)	Oxenius2002b
	• Epitope name: DCK • Using previously defined epitopes [Oxenius2000, Oxenius2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI). • STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.				
p24 (199–218)	Gag (331–350)	KTILRALGPGATLEEMMTAC	HIV-1 infection	human	Novitsky2002
	• HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
p24 (211–230)	p24 (345–364 SF2)	LEEMMTACQGVGGPGHKARV	HIV-1 infection	human	vanBaalen1993
	• Gag CTL epitope precursor frequencies estimated, peptide mapping				
p24 (211–230)	p24 (343–362 SF2)	LEEMMTACQGVGGPGHKARV	HIV-1 infection	human (B7)	McAdam1998
p24 (211–231)	p24 (343–362 SF2)	LEEMMTACQGVGGPGHKAR-VL	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag • One of these 12 had CTL response to this peptide • The responding subject was HLA-A1, A2, B50, B57				
p24 (217–227)	p24 (349–359 IIIB)	ACQGVGGPGHK	HIV-1 infection	human (A*1101)	Brander2001
	• C. Brander notes this is an A*1101 epitope				
p24 (217–227)	Gag (349–359)	ACQGVGGPGHK	HIV-1 infection	human (A*1101)	Fukada2002
	• Counterparts for eight known clade B HLA A*1101 epitopes were generated for clade E (CRF01). Three epitopes, identical among clade A-E, were cross-reactive and recognized by clade E infected individuals. The clade E and B analogs to three more HLA A*1101 epitopes was recognized in a clade specific manner. Two other HLA A*1101 clade B defined epitopes were found not to have stimulated a response in clade E infected individuals. • ACQGVGGPGHK was found to elicit clade-specific responses in clade B (ACQGVGGPGHK is most common in clades A and B) and clade E (acqgvggpShk is most common and is also common in clades C and D). ACQGVGGPGHK was recognized by CTL from 4/5 B clade infected Japanese subjects, and acqgvggpShk from 3/7 E clade infected Thai subjects.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The binding of the two variants to HLA A*1101 was almost identical, but bulk CTL generated from individuals did not cross-react with the cross-clade peptides, indicating the lack of cross-reactivity was due to TCR specificity.				
p24 (217–227)	p24 (349–359 IIIB)	ACQGVGGPGHK	HIV-1 infection	human (A11)	Sipsas1997
	• HIV IIIB proteins were used to define the range of CTL epitopes recognized by three lab workers accidentally infected with HIV-1 IIIB • ACQGVGGPSHK, a variant found in HIV RF, was also recognized				
p24 (217–227)	p24 (SF2)	ACQGVGGPGHK	HIV-1 infection	human (A11)	Goulder2000a
	• The CTL-dominant response was focused on this epitope in a HIV+ Caucasian living in Boston – this epitope did not fall within the three most recognized peptides in the study • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK(p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa			
p24 (217–227)	p24 (349–359)	ACQGVGGPGHK	HIV-1 infection	human (A11)	Oxenius2000
	• Epitope name: ACQ • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable • Both of the 2/8 HLA-A11 study subjects recognized this CTL epitope • Patient SC19(HLA A11/12, B8/44, Cw06/0701, DR3/7, DR52/53, DQ 2/8) had a CTL response to epitopes FLKEKGGL, GEIYKRWII, ACQGVGGPGHK, AVDLSHFLK, and FNCGGEFFY that declined during therapy initiated at day 197 • Patient SC18(HLA A2/11, B8/44, Cw06/0701, DR3/7, DR52/53, DQ2) recognizes the epitopes ACQGVGGPGHK, QVPLRPMTYK, AVDLSHFLK, and one called QIY but not fully described – he had brief therapy upon seroconversion and has had low viral load during 600 days of follow up			
p24 (217–227)	p24 (216–226)	ACQGVGGPGHK	HIV-1 infection	human (A11)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
p24 (217–227)	p24 (349–359 SF2)	ACQGVGGPGHK	HIV-1 infection	human (A11)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-A11+ individuals that had a CTL response to this epitope broken down by group: 0/3 group 1, 0/0 group 2, and 2/2 group 3				
p24 (217–227)	p24	ACQGVGGPGHK	HIV-1 infection	human (A11)	Oxenius2002b
	• Epitope name: ACQ • Using previously defined epitopes [Oxenius2000, Oxenius2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI).				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.				
p24 (221–231)	p24 (353–363 LAI)	VGGPGHKARVL	HIV-1 infection	human (B7)	Mollet2000
	• Epitope name: G1 • A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses • In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished • Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change				
p24 (223–231)	p24 (223–231 SF2)	GPGHKARVL	HIV-1 infection	human (B*0702)	Altfeld2001a
	• Epitope name: GL9 • HIV+ individual AC-06 was tested for reactive overlapping peptides spanning all HIV-1 proteins in an ELISPOT and was found to react with 12 peptides from 7 proteins, suggesting that the breadth of CTL responses are underestimated if accessory proteins are not included in the study • The response to GPGHKARVL was dominant				
p24 (223–231)	p24 (355–363 LAI)	GPGHKARVL	HIV-1 infection	human (B7)	Goulder1997e, Goulder1997a
	• Identical twin hemophiliac brothers were both infected with the same batch of factor VIII • One had a strong response to this peptide, the other a weak response • [Goulder1997a] is a review of immune escape that summarizes this study				
p24 (223–231)	p24 (SF2)	GPSHKARVL	HIV-1 infection	human (B7)	Goulder2000a
	• The CTL-dominant response was focused on this epitope in a HIV+ Caucasian living in Boston – this epitope did not fall within the three most recognized peptides in the study • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK(p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa			
p24 (223–231)	p24 (SF2)	GPSHKARVL	HIV-1 infection	human (B7)	Goulder2000a
	• The CTL-dominant response was focused on this epitope in a HIV+ Caucasian living in Boston – this epitope did not fall within the three most recognized peptides in the study • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK(p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa			
p24 (223–231)	(LAI)	GPGHKARVL		(B7)	Brander2001, Goulder1999a

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (223–231)	p24 (223–231 SF2)	GPGHKARVL	HIV-1 infection	human (B7)	Altfeld2001b
• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-B7+ individuals that had a CTL response to this epitope broken down by group: 1/4 group 1, 2/3 group 2, and 0/1 group 3					
p24 (223–231)	p24 (223–231)	GPGHKARVL	HIV-1 infection	human (B7)	Day2001
• The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person • Subjects with chronic HIV-1 infection recognized between 2-8 out of 11 B7-restricted epitopes • An acute seroconvertor homozygous for the B7 allele recognized five B7-restricted epitopes • The other acute seroconvertor failed to recognize any of the 11 B7-restricted epitopes tested • The B7-restricted CTL response was highly variable and there was no clearly dominant epitope					
p24 (223–231)	p24 (223–231)	GPGHKARVL	HIV-1 infection	human (B7)	Yu2002a
• Epitope name: B7-GL9 • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • Only two epitopes were detected during acute infection in patient AC-06, B7 restricted gp41 epitope IPRRIRQGL and Gag GPGHKARVL. GPGHKARVL was the first targeted peptide, and remained immunodominant through the 34 month study period. • 3/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. 1/4 individuals had detectable responses to this epitope after STI.					
p24	p24 (C consensus)		HIV-1 infection	human	Goulder2000a
• The CTL-dominant response was focused on this epitope in a HIV+ South African – this epitope did not fall within the five most recognized peptides in the study • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK(p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa					

II-B-4 p24-p2p7p1p6 CTL Epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24-p2p7p1p6 (223–1)	Gag	GPGHKARVLA		human (B7)	De Groot2001
	• The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes • A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes were identified that could stimulate IFNγ production in an ELISPOT assay • GPGHKARVLA was confirmed as an HLA-B7 epitope in this study, and had been previously published				
p24-p2p7p1p6 (225–8)	Gag (357–372 LAI)	GHKARVLAEATLSQVN	HIV-1 infection	human	Buseyne1993a
	• Vertical transmission of HIV ranges from 13% to 39% • Primary assays showed cytotoxic activity against at least one HIV protein was detected in 70% of infected children • Epitopes recognized in five children were mapped using synthetic peptides and secondary cultures • Patient EM28 (CDC P2A) had a CTL response to four epitopes in Gag				
p24-p2p7p1p6 (230–7)	Gag (386–)	VLAEAMSQV	HIV-1 infection	human (A*0201)	Altfeld2001c
	• Epitope name: Gag-386 • HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested • Three additional previously described HLA-A2 epitopes were added to the set of 20, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acute infected individuals recognized at least 1 (median of 1 and maximum of 2) • VLAEAMSQV binds to all five HLA-A2 supertype alleles tested: A*0201, A*0202, A*0203, A*0206 and A*6802 (highest affinity) • 4/22 individuals with chronic HIV-1 infection recognized this epitope, and it was immunodominant in 3/4 by ELISPOT • 0/12 acutely infected individuals recognized this epitope				
p24-p2p7p1p6 (230–7)		VLAEAMSQV	HIV-1 infection	human (A02)	Sabbaj2002b
	• Epitope name: Gag-VV9 • Among HIV+ individuals who carried HLA A02, 3/29 (10%) recognized this epitope				
p24-p2p7p1p6 (230–7)	Gag (397–405)	VLAEAMSQV	HIV-1 infection	human (A2 supertype)	Propato2001
	• Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus • This epitope can bind all five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802)				

II-B-5 p2p7p1p6 CTL Epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p2p7p1p6 (5–13)	Gag (SF2)	SQVTNPANI	Vaccine	murine BALB/c (H-2D^b)	Paliard1998
	Vaccine *Strain:* SF2 *HIV component:* Gag • HIV-1(SF2)p55gag vaccination of H-2 mice activates a CTL response against this epitope • CTL that recognized SQVTNPANI in the context of H-2D^b cross-reacted with H-2 alloantigens H-2L^d and an unidentified self-peptide • A postulate: heterozygosity at the MHC level could prevent the maturation of some T cell receptor combinations for foreign peptide and self-MHC constructs because of thymic depletion and tolerance				
p2p7p1p6 (18–37)	Gag (96ZM651.8)	SNFKGNKRMVKCFNCGKEGH		human (A*02011)	Novitsky2001
	• This study is provides a survey of CTL responses and full length HIV-1 genome sequences from a C subtype infected Botswanan cohort • 4 of 8 individuals (50%) who were positive for HLA-A*02011 responded to the peptide SNFKGNKRMVKCFNCGKEGH				
p2p7p1p6 (42–50)	p15 (42–50 SF2)	CRAPRKKGC	HIV-1 infection	human (B14)	Yu2002b
	• 26/57 HIV-1 infected subjects displayed Gag p15-specific CD8+ T-cell IFNgamma responses were measured by Elispot and intracellular staining. The immunodominant regions targeted by CD8+ T-cells were mapped to three functional domains: the zinc finger structures, the protease cleavage site p7/p1, and to the Vpr binding site in p6. • p15 contributed on average 17% of the total Gag response (rage 0-100%). • 3 optimal CTL epitopes were mapped within p15: KELYPLTSL, CRAPRKKGC, and FLGKIWPSYK. • 2/6 HLA-B14+ subjects recognized this epitope. The binding motif for B14 is C-term Cys, positions 2 and 5 Arg.				
p2p7p1p6 (55–70)	p15 (446–460 BRU)	KEGHQMKDCTERQANF	HIV-1 infection	human (A2)	Claverie1988
	• One of 4 epitopes first predicted, then subsequently shown to stimulate an HLA-A2 restricted CTL line				
p2p7p1p6 (64–71)		TERQANFL	HIV-1 infection	human (B*4002)	Sabbaj2002b
	• Epitope name: Gag-TL8 • This study monitored epitope responses in HIV-1 infected minority women living in the United States • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release • This epitope was newly defined in this study • Patient 01RCH59 was Hispanic, not on HAART, and had a viral load of 5100 and CD4 count of 349 – she also recognized AEWDRVHPV, p24(78-86), HLA-B*4002 and KEKGGLEGL, Nef(92-100), HLA-B*4002 • Among HIV+ individuals who carried HLA B40, 3/5 (60%) recognized this epitope				
p2p7p1p6 (70–79)	p15 (70–79 SF2)	FLGKIWPSYK	HIV-1 infection	human (A*0201)	Yu2002b
	• 26/57 HIV-1 infected subjects displayed Gag p15-specific CD8+ T-cell IFNgamma responses were measured by Elispot and intracellular staining. The immunodominant regions targeted by CD8+ T-cells were mapped to three functional domains: the zinc finger structures, the protease cleavage site p7/p1, and to the Vpr binding site in p6. • p15 contributed on average 17% of the total Gag response (rage 0-100%). • 3 optimal CTL epitopes were mapped within p15: KELYPLTSL, CRAPRKKGC, and FLGKIWPSYK. • FLGKIWPSYK was embedded in a peptide recognized by 14/57 (25%) of subjects. • 13/24 (54%) of HLA-A*0201+ subjects recognized this peptide.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p2p7p1p6 (83–97)	Gag (453–462 BH10, LAI)	GNFLQSRPEPTAPPF	HIV-1 infection	human	Maksiutov2002
	• This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins. • This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is PEPTAPPFLQ) has similarity with the T-cell surface glycoprotein CD5, fragment PEPTAPPRLQ.				
p2p7p1p6 (83–97)	p15 (418–433 BRU)	GNFLQSRPEPTAPPF	HIV-1 infection	human (A2)	Claverie1988
	• One of 4 epitopes first predicted, then subsequently shown to stimulate an HLA-A2 restricted CTL line				
p2p7p1p6 (118–126)	p2p7p1p6 (118–126)	KELYPLTSL		human (B*4001(B60))	Brander2001
	• C. Brander notes that this is a B*4001 epitope				
p2p7p1p6 (118–126)	p15 (118–126 SF2)	KELYPLTSL	HIV-1 infection	human (B60, B*4001)	Yu2002b
	• Epitope name: p15-24 • 26/57 HIV-1 infected subjects displayed Gag p15-specific CD8+ T-cell IFNgamma responses were measured by Elispot and intracellular staining. The immunodominant regions targeted by CD8+ T cells were mapped to three functional domains: the zinc finger structures, the protease cleavage site p7/p1, and to the Vpr binding site in p6. • p15 contributed on average 17% of the total Gag response (rage 0-100%). • 3 optimal CTL epitopes were mapped within p15: KELYPLTSL, CRAPRKKGC, and FLGKIWPSYK. • Four patients who were HLA-B60+ recognized KELYPLTSL. • The binding motif for B60 is C-term Leu and 2nd position Glu. • Four patients who did not carry HLA-B60 also recognized the 15 amino acid long peptide carrying KELYPLTSL, suggesting other epitopes in this immediate region can be presented by other HLA class I molecules.				
p2p7p1p6 (121–130)	Gag (484–493)	YPLTSLRSLF	HIV-1 infection	human (B7)	Jin2000b
	• This B7 epitope is one of three subdominant CTL responses detected in a long-term non-progressor • A dominant B7 epitope was defined using conventional methods, and three additional sub-dominant HLA B7 epitopes were defined by first using a non-anchor based strategy, EpiMatrix, to identify 2078 possible epitopes in the autologous HIV-1, followed by B7 anchor residue prediction to narrow the set to 55 peptides for experimental testing				

II-B-6 Gag CTL Epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Gag	Gag (IIIB)		Vaccine	Rhesus macaque	Paliard2000
	Vaccine *Vector/Type:* virus-like particle *HIV component:* gag				
	• CTLs primed by HIV-1 p55 gag virus-like particle (VLP) vaccination recognized epitopes in four different 20 amino acid peptides p17/4, p17/8, p24/13 and p14/9				
	• Cytotoxic T cell response lasted greater than 8.5 months				
Gag	Gag (IIIB)		HIV-1 infection	human	Wasik2000
	• HIV+ infants that progressed rapidly to AIDS had lower Th1 responses and decreased production of beta-chemokines and IL-2 relative to other HIV+ infants				
	• No HIV+ infants had no demonstrable CTL at birth, but Th1 responses accompanied by CTL responses developed in children with slowly progressive disease, and not in rapid progressors				
	• CTLp frequencies were determined by limiting dilution using autologous B cells infected with vaccina/HIV constructs				
Gag	Gag (LAI)		Vaccine	human	Salmon-Ceron1999
	Vaccine *Vector/Type:* canarypox *Strain:* LAI, MN *HIV component:* gp41, Gag, Pro, V3				
	• The vaccine used was a rec canarypox with HIV-1 gp120 MN, tm/gag/protease LAI (vCP205), alone or with p24E-V3 MN synthetic peptide (CLTB-36))				
	• Twenty HIV negative subjects were vaccinated in phase I trial with combinations of vCP205 and CLTB-36				
	• Immunization with vCP205 induced HIV-1-specific ABs to gp120, V3, and p24 antigens, and CTL immune responses against vCP205 were detected after the fourth immunization in 33% of the subjects against Env, Gag and Pol, but the CLTB-36 peptide did not produce AB or CTL immune responses against p24 or gp160				
Gag	p24		Vaccine	human	Klein1997
	Vaccine *Vector/Type:* virus-like particle *HIV component:* p24, p17				
	• Immunization of HIV+ people with an HIV-1 p17/p24 Ty virus-like particle (p24-VLP) resulted in a marginal, short-lived increased proliferative response to p24 and p17 and a transient elevation in viral load				
	• Two of four subjects that received 500 or 1000 μg of p24-VLP had an increase in gag-specific CTL				
Gag	p24 (SF2)		Vaccine	murine, baboon	O'Hagan2000
	Vaccine *Vector/Type:* DNA *Strain:* SF2 *HIV component:* gp120, p24 *Adjuvant:* PLG-microparticle, MF59 adjuvant				
	• PLG (Polylactide co-glycolide polymer) microparticles administered in MF59 emulsion induced gp120 Ab responses and CTL immune responses against p24 gag				
Gag	Gag		HIV-1 infection	human	Lubaki1999
	• Three strategies were used to analyze CTL activity: area under the net HIV-specific lysis curve (ACU), linear regression (LR) of net specific lysis, and the standard method, lytic units (LU20)				
	• A correlation between low HIV plasma viral load and increased levels of HIV-specific Gag and Nef CTL activity was observed using ACU and LR, but not LU20				
Gag	Gag		HIV-1 infection	human	Kalams1999a
	• The presence of HIV-1 p24-specific proliferative responses was positively correlated with Gag-specific memory CTL and negatively correlated with viral load in untreated subjects				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Gag proliferative responses were the most readily detected – Gag CTL responses were the only responses with a significant correlation with Gag stimulated help, although there was a positive trend with Nef, Env and RT				
Gag	p55 (IIIB)		HIV-1 infection	human	Greenough1999
	• 7/128 HIV-1 infected hemophiliac were identified as long-term non-progressors (LTNPs) and were monitored for viral and host immune parameters over 15 years – LTNPs maintained a low viral load, high frequencies of CTL precursors directed against Gag antigen and low levels of HIV-specific effector CTL activity – effector cell activity suggests low level ongoing viral replication				
Gag	Gag		HIV-1 infection	human	Trickett1998
	• Twelve HIV-1 infected patients were re-infused with their own lymphocytes, cryopreserved from an earlier time point in the infection • Improvement in CD4+ and CD8+ T cells was seen in 7/12, and an increase in the CTL response to Gag was seen in one patient				
Gag	Gag (IIIB)		HIV-1 infection	human	Betts1999
	• This study demonstrated an inverse correlation between HIV Type I plasma viral load and CTL activity directed against HIV-1 Pol, and stronger combined effects of Pol- and Env-specific CTL, in long-term survivors (LTS) of HIV-1 infection				
Gag	Gag (LAI)		HIV-1 infection	human	Legrand1997
	• Seventeen recently infected patients were tested for CTL response to HIV proteins Env, Gag, Pol, Rev, Nef, Vif and Tat • An early response (within a month following PI) was noted in 87% of the subjects to Gag, 75% to Env, and 50% to Nef • Early responses to Pol, Rev, Vif and Tat were rare				
Gag	Gag (IIIB)		HIV-1 infection	human	Betts1997
	• 6/8 individuals from Zambia infected with C clade virus had CTL that were able to make response to B clade HIV-1 IIIB vaccinia-expressed Gag, Pol and Env proteins • A vigorous cross-clade response was not limited to a particular protein, and the level of recognition of different proteins varied among the six patients				
Gag	Gag		HIV-1 infection	human	De Maria1997
	• CD3+ cells that also carry a natural killer cell receptor (NKR+) can exhibit down regulation of T cell function • Anti-NKR IgM MAb masked this inhibitory function and increased HIV-1 specific CTL activity in phytohemagglutinin-activated PBMC cultured in the presence of IL-2 from 3/5 patients, and in one other case anti-NKR MAb brought HIV-1 specific CTL activity to detectable levels				
Gag	Gag (LAI)		Vaccine	human	Belshe1998
	Vaccine *Vector/Type:* canarypox prime with rgp120 boost *Strain:* MN, LAI, SF2 *HIV component:* gp120, gp41, Gag, Protease • The live canarypox vaccine ALVAC-HIV(vCP205) carrying MN gp120, LAI gp41, Gag and Protease, and boosted with SF-2 rpg120, was given to HIV-1 seronegative volunteers – HIV-specific Env or Gag CD8+ CTL were detected in 64% of the volunteers				
Gag	Gag (LAI)		HIV-1 infection	human	Buseyne1998a
	• This study showed a correlation between strong CTL memory and breadth of response in 7-12 month old infants, and remaining AIDS-free for the first year of life, higher absolute CD4 and CD8 cells, and lower viral load				
Gag	Gag (LAI)		HIV-1 infection	human	Buseyne1998b
	• In infants with positive CTL responses, most responses showed cross-clade reactivity with somewhat diminished recognition of epitopes from different subtypes				
Gag	Gag		HIV-1 exposed seronegative	human	Goh1999
	• 13/37 exposed uninfected individuals with repeated high-risk sexual exposure had HIV-1 specific CTL against Env, Gag, Pol, or a combination of proteins – CTL activity was correlated with a CCR5 wildtype genotype				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• In this group, the highest CTLp frequencies were directed at Gag, but the most common response was to Env and four individuals had responses to multiple HIV-1 proteins				
Gag	Gag (LAI)		Vaccine	human	Evans1999
	Vaccine *Vector/Type:* canarypox *HIV component:* gp120, gp41, Gag, Pro, Nef, RT				
	• A Canarypox vaccine expressing gp120, gp41, Gag, Protease, Nef and Pol CTL epitopes gave rise to CTL that could be detected in 61% of the volunteers – responses to Gag, Env, Nef and Pol were detected 3-6 months after the last vaccination				
Gag	p17		HIV-1 infection	human	Kuiken1999
	• A correlation between conserved regions of p17 or Nef and CTL epitope density was noted – the authors suggest that this may be due to a biological reason such as epitope processing, or may possibly be an artifact of experimental strategy for epitope definition such that conserved epitopes would tend to be identified because they would be more likely to be cross-reactive with the test reagents				
	• In contrast to p17 and Nef, p24 is a more conserved protein and known epitopes are evenly distributed across p24				
Gag	Gag (LAI)		Vaccine	Macaca nemestrina	Kent1998
	Vaccine *Vector/Type:* DNA prime with vaccinia boost *Strain:* LAI *HIV component:* Env, Gag				
	• Priming with an HIV-DNA vaccine and boosting with a vaccinia construct induced greater levels of HIV T cell immunity than either vaccine alone				
	• The proliferative response to Env and Gag after the DNA vaccination had a mean SI of 1.5-4, but after boosting with rHIV-fowlpox virus, there was a 6-17 fold increase in the mean SI for HIV Gag and Env. The T help response happened despite a fall in antibody titers, suggesting that the Th response was primarily Th1, not Th2. The CTL response was also enhanced				
Gag	Gag/Pol (LAI, MN)		Vaccine	human	Salmon-Ceron1999
	Vaccine *Vector/Type:* canarypox *Strain:* MN, LAI *HIV component:* gp120, gp41, Gag, Protease				
	• A live attenuated canarypox vector expressing MN gp120 and LAI gp41/gag/protease could induce CTL and a lymphoproliferative response in healthy, uninfected volunteers				
Gag	Gag/Pol (MN)		Vaccine	chimpanzee	Kim1998
	Vaccine *Vector/Type:* DNA *HIV component:* Env, Gag, Pol *Adjuvant:* CD86, CD80				
	• The study explores the use of co-stimulatory molecules co-expressed with an HIV-1 immunogen in a DNA vaccine to enhance the immune response – co-expression of CD86, but not CD80, dramatically increased both HIV Env and Gag/Pol specific CTL and Th proliferative responses				
Gag	Gag (BRU)		HIV-1 infection	human	Aladdin1999
	• In vitro measurements of CTL-activity by Cr release assay in bulk culture showed no correlation between CTL-activity (gp120, Gag, Pol and Nef) and disease progression as measured by viral load, CD4 and time to death				
Gag	Gag		Vaccine	Rhesus macaque	Akahata2000
	Vaccine *Vector/Type:* DNA *Strain:* ZF1 *HIV component:* complete genome				
	• Rhesus macaques were vaccinated by i.m. injection with naked plasmid DNA carrying an HIV-1 complete genome vaccine, strain ZF1, with a mutated zinc finger in the nucleocapsid to prevent packaging				
	• Env and Gag specific CTL but no antibody responses were induced in 2/4 vaccinated monkeys (MM145 and MM153)				
	• 2/4 monkeys (MM146 and MM143) produced antibodies against p24 and/or gp160, but no CTL response was detected				
	• PBMC from all vaccinated monkeys produced IFN-gamma, in response to HIV-1 gp160, indicating a Th response – this response was 5 times higher in MM145, the animal with the strongest CTL response				
	• 4 weeks post-challenge with SHIV NM-3rN plasma viral loads of both MM145 and MM153 (with a homologous Env) decreased to near or below the detection limit				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• 6-8 weeks post-challenge with SHIV NM-3rN plasma viral loads of both MM146 and MM143 decreased near or below the detection limit				
Gag	Gag		HIV-1 infection	human	Salerno-Goncalves2000
	• A general test of CD8 anti-viral activity was developed based on proviral load of coculture of autologous CD8+ cells with CD4+ cells after homogeneous superinfection with NSI virus • Significantly decreased the CD4+ T-cell proviral loads were found in 12 HIV+ slow progressors relative to 10 rapid progressors • Significant CD8+ mediated cytotoxicity directed against autologous cells infected with vaccinia carrying the HIV-1 gag gene was observed in slow progressors in contrast to rapid progressors, but no correlation was found between plasma viral load in 22/22 asymptomatic HIV infected individuals				
Gag	Gag		HIV-1 infection	human	Young2001
	• Addition of recombinant rec human IL12 (rhIL12) to cultures increased HIV-specific lysis of HIV-Gag, Pol and gp120 vaccinia expressed antigens (11/15 tested increased lysis by > 5%) if the culture was derived from HIV+ individuals who had CD4 cells/ul > 500 • 2/10 individuals with <200 CD4 cells/ul, and 3/10 individuals with 200-500 CD4cells/ul, had an increase of >5% upon treatment of the culture with rhIL12, so a few individuals in late stage disease had CD8 cells that maintained responsiveness to rhIL12				
Gag	p24		HIV-1 infection	murine	deQuiros2000
	• CB-17 SCID-Hu mice engrafted with peripheral blood mononuclear cells of four long-term nonprogressors (viral load < 50 copies/ml) displayed resistance to challenge with HIV-1 SF162, mediated by CD8+ T-cells and associated with proliferation in response to p24 – these patients did not have a higher level of HIV-1 specific immunity in vitro, so the mechanism is unknown				
Gag	Gag (subtype A, B, D)		HIV-1 infection	human	Cao2000
	• HIV-1 subtypes A and D dominate the Ugandan epidemic, and a vaccine trial using B clade antigen is underway – this study addresses relative levels of cross-reactive CTL responses in HIV infected Ugandans to A, D, and B clade recombinant vaccinia viruses expressing Gag, Env, RT or Nef from HIV-1 clades A, B, and D; =Proteins corresponding to the subtype of the infecting strains tended to trigger higher levels of CTL response measured by percent specific lysis, but there was extensive inter-subtype cross-reactivity with B clade proteins and the co-circulating subtype				
Gag	Gag		HIV-1 infection	human	White2001
	• HIV-specific CTL activity was detected in the female reproductive tract of only 1/3 HIV-infected women who underwent a hysterectomy, although CTL could be identified in the PBMC of all three women				
Gag	Gag (HXB2)		HIV-1 infection	human	Chun2001
	• Suppression of viral replication in the resting CD4+ T-cell reservoir by autologous CD8+ T-cells via CD4+/CD8+ cell contacts was observed in long-term nonprogressors and patients undergoing antiretroviral treatment, but this activity appears to be independent of Gag-specific CTL activity				
Gag	Gag (IIIB)		HIV-1 infection	human	Jin2000a
	• The CTL precursor level (CTLp) was measured in long term non-progressors (LTNP) with low viral load using limiting dilution analysis and measuring CTL against Env Gag and Pol expressed in vaccinia in autologous targets • LTNPs have high memory CTL numbers and low viral load				
Gag	Gag		HIV-1 exposed seronegative	human	Rowland-Jones2001
	• This is a review that summarizes observations about HIV-specific CTL found in the HIV-1 exposed persistently seronegative (HEPS) population • The CTL responses assayed by ELISPOT and by CTL precursor frequencies by limiting dilution analysis indicate that CTL in HEPS individuals tend to be of a lower magnitude than in chronic HIV-1 infections – the responses in HEPS cases are below the level of detection by tetramer assays • CD8+ CTL responses tend to be detectable in HEPS subjects only if they are recently exposed, and the response diminishes if exposure is reduced – it is not clear if there is a stable memory population in HEPS cases				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• CD8+ CTL responses in the HEPS population are associated with HIV-1 specific CD4+ T cell responses, assayed by proliferation assays, IL-2 secretion, and ELISPOT, and the authors consider the possibility that HIV-1-specific T-help responses improve the "quality" of the CD8+ response in HEPS individuals relative to HIV-1 infected individuals, who tend to have a poor HIV-1-specific T-help response • HIV-1 specific CD8+ CTL responses in HIV-1 infected individuals show reduced levels of perforin, and the T cells may not mature properly, and although similar studies have not been conducted in HEPS individuals this is considered as a possible difference in the CTL immune response in HEPS and HIV-1 infected people				
Gag			Vaccine	murine	Nabel2002
	Vaccine *Vector/Type:* DNA *HIV component:* Gag, Pol, Env, Gag-Pol fusion protein, Gag-Pol pseudoparticle • Using DNA that had humanized codon usage, CTL responses to DNA vaccines containing either Gag, Pol, Gag-Pol fusion protein, or Gag-Pol pseudoparticles suggested that the greatest breadth and most potent response was to the Gag-Pol fusion protein. The Gag-Pol fusion lacks the Gag precursor protein required for viral assemble, so does not form releaseable particles; the author speculates that longer retention of the Gag-Pol protein with in the cell may enhance antigen presentation.				
Gag			HIV-1 exposed seronegative	human	De Maria1994, Kuhn2002
	• 6/24 HIV uninfected infants (ages 15-50 months) born to HIV+ mothers had HIV-1 specific CTL responses to vaccinia-expressed Nef, Gag/Pol, Env. • Reviewed in [Kuhn2002].				
Gag			HIV-1 infection	human	Aldhous1994, Kuhn2002
	• Six of nine HIV vertically infected infants had HIV-1 specific CTL responses to vaccinia expressed Tat (4/6), Pol (6/6), Env (1/6), or Gag (1/6), but not all responses were detected at all time points. • Two of eleven babies that were not infected though born to HIV+ mothers had detectable responses to Tat (1/2), Pol (2/2), Gag (1/2). • Reviewed in [Kuhn2002].				
Gag			HIV-1 infection	human	Kuhn2002, Wasik1999
	• In HIV-infected infants HIV-specific, CTL responses were not detectable in icord blood or in PBMC collected shortly after birth and were absent or remained very low in 3 infants with a rapidly progressive disease. For those who progressed more slowly, the HIV-specific CTL activity varied. • The two infants with high levels of Env peptide-stimulated IL-2 responses had the highest CTLp frequencies. • Stronger responses were detected after initiation of the antiretroviral therapy. • Two babies that were not infected though born to HIV+ mothers had detectable though low HIV-specific CTLp responses to Env (1/2), Pol (2/2), Gag (1/2) cord blood and transiently in PBMC after birth. • Reviewed in [Kuhn2002].				
Gag			HIV-1 infection	human	Kuhn2002, McFarland1994
	• Only 9% of HIV+ infants had HIV-specific CTL against Env or Gag in unstimulated PBMC. After CD3 stimulation of PBMC, Gag and Env specific CTL were found in PBMC from 91% and 78% of HIV-infected children, respectively, with high precursor frequencies. • Reviewed in [Kuhn2002].				
Gag			HIV-1 infection	human	Yusim2002
	• Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17. • In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed. p17 is much more variable than p24.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Gag	p24 (HXB)		HIV-1 infection	human	Lu2000a
• Bacillus anthrax lethal toxin (LFn)-HIV fusion proteins are candidate HIV vaccines that are safe in mice, and LFn-V3 region fusion proteins induce CD8 T cells in BALBc mice. LFn causes exogenous protein to be taken up and processed in a class I pathway. Expressed proteins from Gag p24 and Nef fragments cloned into the LFn expression plasmid stimulate gag-specific CD4 proliferation and CTL responses in HIV-infected donor PBMCs in vitro.					
Gag	(HXB2)		HIV-1 infection	human	Edwards2002
• 96% (26/27) chronically infected HIV-1 infected patients elicited gamma-IFN CD8+ T-cell responses against Gag • Nef and/or Pol CTL responses were detected in 86% of the subjects • The magnitude and breadth of Gag and p24 T-cell responses correlated with absolute CD4 counts, and inversely correlated with viral load • Pol and Int CTL responses correlated positively with absolute CD4+ T-cell count • Nef and Env responses did not correlate with either CD4 counts or viral load					
Gag			HIV-1 infection	human	Larsson2002b
• Autologous mature dendritic cells with rec vaccinia expressing Gag, Pol, Nef and Env could amplify CD8+ T-cell Elispot responses 4-38 fold in five HIV+ patients on successful HAART treatment, relative to autologous monocytes. Some weak responses could only be detected using mature dendritic cells as APCs, and this approach could be useful for detection of low frequency memory cells.					
Gag	(IIIB)		HIV-1 infection	human	Trickett2002
• Conditions were optimized for ex-vivo expansion of CD8+ and CD4+ T-cells with the goal of functional T-cell production for autologous immunotherapy. 10,000-fold expansions were obtained in 14 days with optimized concentrations of IL-2, anti-CD3 and anti-CD28 coated microspheres, and decreasing amounts of serum over the first 8 days.					
Gag	(IIIB)		HIV-1 and HCV co-infection	human	Lauer2002
• HIV-1 and HCV immune responses were studied in 22 individuals who were co-infected with HIV-1 and hepatitis C virus (HCV). IFNgamma production was measured in an Elispot assay of CD8+ T-cells using targets expressing either Gag, RT, Env and Nef in a vaccinia construct, or one of seven HCV proteins. • All 22 patients targeted at least one protein. 20/22 patients recognized RT, 17/22 patients recognized Gag, 13/22 subjects recognized Env and 11/22 patients recognized Nef. Robust CTL activity was independent of disease progression or viral load. • Despite high HCV viral loads, very few HCV CD8+ T-cell Elispot responses were detected. In a control HCV infected person who did not have HIV-1, strong anti-HCV responses were mounted. • HIV-specific CD4 proliferative responses were detected in 9/17 coinfected patients, but no HCV responses were detected.					
Gag			HIV-1 infection	human	Luzuriaga1995
• 2/3 infants infected in utero had detectable HIV-1 Gag and Env specific CTL responses, one by 4 months, one by 11 months of age. Levels of the responses varied at different time point. Pol responses were not detected. • 2/4 infants infected intrapartum had detectable responses, one note until 11 months, one not until 42 months. • HIV-specific CTL were not detected in ten HIV- infants that were born to HIV+ mothers.					
Gag			Vaccine	human	Gupta2002
Vaccine *Vector/Type:* canarypox prime with rgp120 boost *Strain:* Gag, LAI; gp120, MN; and gp41, LAI *HIV component:* gag, env • A safety and immunogeniticity study of a vaccine dosing schedule was studied in a trial conducted in high and low risk study subjects. There was a 76% cumulative probability of detecting a Gag or Env CTL response by day 728.					
Gag			HIV-1 infection	human	Scott2001
• CTL responses before and after initiation of ART were studied in 13 HIV-1 vertically infected infants <6 months of age, and 4 that were >6 months of age.					

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Before ART 2/13 infants <6 months of age showed IFNgamma Elispot CD8+ T-cell responses, one to Nef and one to Env and Nef, and these responses became undetectable after successful therapy– 3 infants were coinfected with CMV and all 3 had CMV-specific CD8+ T-cell responses. • One older infant, at 23 months, had CTL responses against all for proteins tested, Gag, Pol, Nef and Env, and had the lowest plasma viremia of the study group. 3/4 infants older than 6 months of age responded to either Nef or Pol. • Administration of ART over 48 weeks broadened the HIV-1-specific CTL response in 2/4 of the older children that were incomplete responders.				
Gag	(IIIB, MN)		HIV-1 infection	human	Larsson2002a
	• Dendritic cells acquire and present HIV-1 antigens derived from dead, apoptotic cells or from non-infectious, fusion-competent HIV-1 virions, and these DC cells could stimulate CD4+ and CD8+ T-cells resulting in IFNgamma production in an Elispot assay. Both HLA Class I and class II molecules were used for presentation. This may be an important aspect of the initial immune response to HIV-1 infection of CD4+ cells in the mucosal subepithelia.				
Gag	(IIIB)		HIV-1 infection	human	Ortiz2001
	• Immune responses in eight chronically HIV-1 infected patients undergoing HAART therapy structured treatment interruptions (STI) were studied. STI boosted HIV-1 specific CTL responses and elevated CTL responses were maintained up to 22 weeks after the last treatment interruption, but viral load rebound to pretreatment levels and CD4 T-cell count decline was observed. CD8 responses in PBMC were measured by cytokine flow cytometry with gp160, Gag p55, RT-Pol and Nef expressed in vaccinia.				
Gag	Gag		HIV-1 infection	human (A*0201 and Cw*08)	Shacklett2000
	• HIV-1 specific, MHC class I-restricted CTL killing was detected in duodenal and rectal gut associated lymphoid tissue (GALT) sites from three infected individuals – the distribution of class I restricted CTL was different in the peripheral blood samples and GALT samples				
Gag			computer prediction	(A*0201, B*3501)	Schönbach2002
	• Computational methods (artificial neural networks, hidden Markov models, binding matrices based on HLA association rates) were used to identify HLA-A*0201 and HLA-B*3501 HIV T-cell epitope candidates from 533 Gag, Env and Pol sequences of which 374 were derived from HIV-1, 97 were derived from HIV-2 and 62 from SIV. Comparisons to known epitopes and between clades were made.				
Gag	Gag		HIV-1 infection	human (B*35)	Jin2002
	• Patients with HLA-B*35 variants B*3502, B*3503, B*3504, and B*5301 tend to proceed to AIDS more quickly than those with B*3501. • Of 32 patients with HLA-B*35 alleles CD8+ CTL responses were quantified using an intracellular cytokine staining assay – 75% had responses to Pol, 69% to Gag, 50% to Nef, and 41% to Env. • The overall magnitude of CTL responses did not differ between those bearing B*3501 and the others. A higher percentage of Gag responses was observed in those that had lower RNA levels that carried B*3501, and there was a negative association with viral load and CTL activity. The data is consistent with higher levels of CTL responses contributing to protection in B*3501 individuals, but not in B*3502, B*3503, B*3504, and B*5301 individuals.				
Gag			Vaccine	human (B60)	Ferrari2001
	Vaccine *Vector/Type:* canarypox prime with rgp120 boost, canarypox prime with rgp160 boost *Strain:* gp41 LAI, Gag LAI, gp120 MN, gp120 SF2 *HIV component:* gp120, gp41, Gag, Pol and Nef epitope rich regions • HLA-B60 responses dominated the responses against an Gag vaccine in an individual (022G0Z) who was HLA A1, A11, B8, B60. The strongest response was against the MN peptide 107-136. Low level Gag responses were observed against B8 and A11 epitopes, no response was observed against A1 epitopes. • Vaccinee 202T7 (HLA A2, B27, C25) made the strongest response to an epitope at positions 131-140 of Gag. The response was highly cross-reactive with D clade Gag expressed from vaccinia, less so with C, and only minimally cross-reactive with A and CRF01.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Gag	p24		Vaccine	murine (H-2^b, H-2^d, H-2^k)	Iroegbu2000

Vaccine *Vector/Type:* DNA *HIV component:* p17/p24

- The p24 sequence is more conserved than is p17 within patient, and nonsynonymous substitutions are spread evenly throughout its coding regions, not concentrated in CTL epitopes
- Minor changes in p24 did not alter the immunogenicity in H-2b,d, or k mice, while changes in p17 (92% similarity) did alter immunogenicity

Gag	p24		Vaccine	murine (H-2^d)	Qiu2000

Vaccine *Vector/Type:* DNA *HIV component:* gag

- Mice were injected with plasmid DNA at 0, 2 and 4 weeks and lymphocyte proliferation was measured after 6 weeks with recombinant p24 protein
- Secreted HIV-1 Gag expression vectors generated a stronger response than standard Gag or cytoplasmic Gag expression vectors
- IFN-gamma levels were increased compared to an undetectable IL-4 response
- CTL levels were also increased in secreted Gag expression vaccination studies

Gag	Gag (SF2)		Vaccine	Rhesus macaque, murine (H-2^d)	zurMegede2000

Vaccine *Vector/Type:* vaccinia *Strain:* SF2 *HIV component:* Gag, Protease, codon-optimized

- Sequence-modified Rev-independent gag and gag-protease gene constructs lead to increased expression levels and elevated CTL and antibody immunogenicity in BALB/c and CB6F1 mice
- A CTL response in mice could be detected after a single immunization with codon-optimized gag, using 2 ng of plasmid; wild type gag required 200 ng to detect a response
- Recognition of 3 different Gag peptide pools was observed, indicating a polyclonal CTL response
- Significant gag-specific CTL responses were detected in 4/4 rhesus monkeys, in contrast to 1/4 using wildtype gag

Gag	p24		Vaccine	murine (H-2^d)	Halim2000

Vaccine *Vector/Type:* coxsackievirus *HIV component:* partial p24, polyepitope

- An avirulent recombinant coxsackievirus (CB4-P) construct was generated that can express p24 Gag sequences – CB4-P is attenuated even in immunodeficient mice and T help responses can be elicited from peptides embedded in a surface loop of the VP1 capsid
- This paper describes the vaccine strategy and generation of constructs, and employs amino-terminal fusion of Gag sequences to the viral polyprotein with subsequent cleavage to elicit CTL responses via MHC class I presentation in BALB/c mice

Gag	Gag		Vaccine	murine (H-2^d)	Huang2001

Vaccine *Vector/Type:* DNA *Strain:* gag HxB2, pol NL43 *HIV component:* Gag, Pol

- Mice were immunized with four humanized DNA constructs: GagPol, that would form a pseudoparticle carrying Gag and Pol, Gag, Pol or a GagPol fusion construct
- The GagPol pseudoparticle, Gag and GagPol fusion construct all elicited strong anti-Gag CTL, but only the GagPol fusion construct elicited strong anti-Pol CTL

Gag	Gag (HXB)		Vaccine	murine (H-2^d, H-2^b)	Mata2001

Vaccine *Vector/Type:* Listeria monocytogenes *Strain:* HXB2 *HIV component:* Gag

- BALB/c and C57BL/6 mice were immunized with recombinant Listeria monocytogenes (Lm-Gag) expressing HIV-1 HXB2 Gag and mice were challenged with vaccinia expressing Gag
- L. monocytogenes is a gram-positive bacteria that enters the macrophage on phocytosis and lives in the cytoplasm – secreted L. monocytogenes antigens are processed and presented by both class I and class II pathways

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• CD4+ Th1 T-cells mediated the Gag specific immunological protection in mice immunized with Lm-Gag and challenged with vaccinia-Gag • Gag-specific CTL may enhance viral clearance via IFN-gamma secretion, but are not essential for immunity;,				
Gag	Gag		Vaccine	murine (H-2^d, H-2^b)	Mata2000
	Vaccine *Vector/Type:* Listeria monocytogenes *Strain:* HXB2 *HIV component:* Gag • BALB/c and C57BL/6 mice were immunized with recombinant Listeria monocytogenes (Lm-Gag) expressing HIV-1 HXB2 Gag and mice were challenged with vaccinia expressing Gag • L. monocytogenes is a gram-positive bacteria that enters the macrophage on phagocytosis and lives in the cytoplasm – secreted L. monocytogenes antigens are processed and presented by both class I and class II pathways • This article is a review of L. monocytogenes biology and its potential as a vaccine vector for HIV, comparing to other vector systems, and discussing CD4+ Th1 T-cells mediated Gag specific immunological protection in mice and the Gag CTL response				
Gag	Gag (SF2)		Vaccine	murine (H-2^{bxd})	Otten2000
	Vaccine *Vector/Type:* DNA, vaccinia *Strain:* SF2 *HIV component:* codon-optimized gag and pol • CB6F1 were primed with gag DNA by im injection and challenged with vaccinia expressing Gag/Pol (rVVgag-pol) • Gag-specific CTL responses were detected by IFNgamma secretion in the spleen, independent of the route (intraperitoneal, intranasal or intrarectal) of rVV gag-pol challenge • The gag DNA vaccine induced CTL responses in 4/4 monkeys 2 weeks post immunization, but antibody responses were detected in only 1/4 monkeys after 3 immunizations • CTL cross-reactivity against Gag sequences 1-80, 254-323, and 421-496 was observed, suggesting multiple CTL epitope recognition				

II-B-7 Gag/Pol CTL Epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Gag/Pol	Gag/Pol (ARV-2 SF2)		Vaccine	Macaca nemestrina	Kent2000
	Vaccine *Vector/Type:* fowlpoxvirus *Strain:* ARV-2,SF2 *HIV component:* Gag, Pol *Adjuvant:* IFN-gamma				
	• Vaccination with FPV Gag/Pol-IFN-gamma increased HIV-1 specific CTL and T cell proliferative responses to Gag/Pol antigens, respectively, in infected Macaca nemestrina				
	• HIV-1 viral loads remained low and unchanged following vaccinations				
Gag/Pol	RT		Vaccine	murine	Kim1997d
	Vaccine *Vector/Type:* DNA *HIV component:* Gag, Pol, Vif, Env *Adjuvant:* B7, IL-12				
	• A Gag/Pol or Env DNA vaccine, when delivered in conjunction with the plasmid encoding the co-stimulatory molecules CD86, gave a dramatic increase in both the cytotoxic and proliferative responses in mice				
	• When CD86 was present, CTL response could be detected even without in vitro stimulation				
Gag/Pol	RT		HIV-1 infection	human	Gamberg1999
	• 13/13 subjects with advanced HIV infections showed CD8 T cell proliferation and differentiation of CTL in vitro, and six individuals showed HIV-specific responses to Gag, Pol, Env or Nef antigens				
	• Data suggests that the functional and genetic integrity of the CD8 T cell repertoire (TCR V beta gene intrafamily genetic diversity) remains intact through advanced HIV infection, although HIV-specific CTL activity decreases				
Gag/Pol			Vaccine	murine	Muthumani2002
	Vaccine *Vector/Type:* adenovirus *HIV component:* Vpr, Nef, Gag/Pol				
	• Vpr can cause cells to go into G2 arrest, and it surpresses immune cell activation and inflammatory cytokine production, so co-immunization of BALB/c mice with recombinant adenovirus expressing Vpr and HIV-1 antigens Nef or Gag/Pol was tested to see if Vpr reduced the immune response to the other HIV antigens.				
	• Vpr compromised CD8+ T-cell lytic responses and T-helper proliferative responses in mice co-immunized with Vpr and Nef or Gag/Pol.				
	• In vitro, Vpr reduced T-cell cytokine production of IL-12 and TNFalpha, indicative of Vpr-mediated immune suppression.				

II-B-8 Protease CTL Epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Protease (3–11)	RT (71–79 subtype A, B, D) • C. Brander notes this is an A*6802 epitope	ITLWQRPLV		human (A*6802)	Brander2001
Protease (3–11)	Pol	ITLWQRPLV	HIV-1 infection, Vaccine	human (A*6802)	Hanke2000, Wee2002
	Vaccine *Vector/Type:* DNA prime with vaccinia MVA boost *Strain:* subtype A *HIV component:* p17, p24, polyepitope • The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000]. • Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].				
Protease (3–11)	Protease (71–79 LAI) • Predicted on binding motif, no truncations analyzed • Clade A/B/D consensus, S. Rowland-Jones, pers. comm.	ITLWQRPLV		human (A*6802, A*7401, A19)	Dong1998a
Protease (3–11)	RT (71–79 subtype A, B, D) • C. Brander notes this is an A*7401 epitope	ITLWQRPLV		human (A*7401)	Brander2001
Protease (3–11)	Pol (59–65) • One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles	ITLWQRPLV	HIV-1 infection	human (A28)	Ferrari2000
Protease (3–11)	RT (71–79 LAI) • Epitope name: P2 • A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses • In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished • Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change	ITLWQRPLV	HIV-1 infection	human (A28supertype)	Mollet2000
Protease (3–11)	Pol • ITLWQRPLV cross-reacts with clades A, B and D	ITLWQRPLV	HIV-1 infection, HIV-1 exposed seronegative	human (A74)	Kaul2001a

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers				
Protease (11–20)	Pol (91–100)	VTILIGGQLK	HIV-1 infection	human (A3 supertype)	Propato2001
	• Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus • This epitope can bind 3/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801)				
Protease (12–20)	Pol (92–100)	TIKIGGQLK	HIV-1 infection	human (A3 supertype)	Propato2001
	• Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus • This epitope can bind 3/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801)				
Protease (30–38)	Pol (subtype B)	DTVLEEMNL	HIV-1 exposed seronegative	human (A*6802)	Rowland-Jones1998b
	• HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes • This epitope is conserved among B and D clade viruses • The Clade A version of the epitope: DTVLEDINL • This epitope was recognized by two different exposed and uninfected prostitutes • This epitope was identified by screening 49 HIV-1 peptides with the predicted A*6802 anchor residue motif x(VT)xxxxxx(VL)				
Protease (30–38)	Pol (subtype A)	DTVLEDINL	HIV-1 exposed seronegative	human (A*6802)	Kaul2000
	• 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 gamma-IFN responses in the cervix – systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses • Low risk individuals did not have such CD8+ cells • CD8+ T cell epitopes: DTVLEDINL (3 individuals), SLYNVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women				
Protease (30–38)	RT (85–93 subtype D)	DTVLEEWNL		human (A*6802)	Brander2001
	• C. Brander notes this is an A*6802 epitope				
Protease (30–38)	Pol (subtype A)	DTVLEDINL	HIV-1 infection	human (A*6802)	Kaul2001c
	• This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative • DTVLEDINL was recognized in 3 of the 6 women (ML857, ML1203, and ML1707), and the response was present in the last available sample prior to seroconversion, 3-7 months				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• In each of the three women, 20/20 sequences of the infecting strain had no substitutions in this epitope, all were DTVLEDINL, so there was no evidence for escape • The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire • This epitope was recognized in 3/22 HEPS sex worker controls, ML851, ML1432, and ML1601				
Protease (30–38)	Pol (85–93)	DTVLEDINL	HIV-1 infection, HIV-1 exposed seronegative	human (A*6802)	Kaul2001a
	• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure • Among HLA-A*6802 women, 11/12 HEPS and 6/11 HIV-1 infected women recognized this epitope likelihood ratio 4.4, p value 0.08, and HEPS women tended to respond to DTVLEDINL, infected women tended to ETAYFYILKL • The dominant response to this HLA allele was to this epitope in 10 of the 11/12 HEPS cases, but in only 4 of the 6/11 HIV-1 infected women • Differences in epitope specificity were only seen for responses restricted by class I HLA alleles A2, A24, A*6802, B14, and B18, previously shown to be associated with resistance to HIV-1 in this cohort • Four epitopes were considered to be "resistant epitopes", as they were preferentially reactive in HEPS women and so may confer resistance, and these were found in three different proteins: A2 ILK(D/E)PVHGV in RT, A*6802 DTVLEDINL in Protease, B14 DLN(M/T)LN(I/V)V in p24 and B18 FRDYVDRF(Y/F)K also in p24 • Subject ML 857 shifted from a A*6802 DTVLEDINL and B35 (H/N)PDIVIYQY response prior to seroconversion to a B35 PPIPVGDIY and B35 VPLRPMTY response post-seroconversion, and the loss of the pre-seroconversion response was not due to sequence variation within these epitopes • Subject ML 1203 started with CTL responses to A*6802 DTVLEDINL and B7 FPVTPQVPLR prior to seroconversion, and upon seroconversion acquired additional responses to A*6802 ETAYFILKL which became dominant, B7 TPGPGV/IRYPL, B7 IPRRIRQGL, and B7 SPRTLNAWV • Subject ML 1707 started with a CTL response to A*6802 DTVLEDINL prior to seroconversion, and switched to A*6802 ETAYFILKL and A24 RDYVDRFFKTL post-seroconversion, and the loss of the pre-seroconversion response was not due to sequence variation within the epitope • Subject ML 1830 made no detectable response prior to seroconversion, but responded to A*6802 DTVLEDINL and A*6802 ETAYFILKL post-seroconversion				
Protease (30–38)	Pol	DTVLEDINL	HIV-1 infection	human (A*6802)	Kaul2002
	• Neisseria gonorrhea cervititis in 9 HIV+ Kenyan sex workers caused a functional deficiency in IFN-gamma production in HIV-1 epitope-specific CD8+ T-cells, detected by intracellular cytokine production and tetramer assays, while not affecting the total number of epitope-specific CTLs. • Ghonorrhea caused the weaker HIV-1 specific CTL responses in 4 HIV-1 exposed persistently seronegative (HEPS) women to become undetectable by Elispot and tetramer assays, and CMV-specific CTL in 2 HEPS subjects were shown to have impaired function with regard to IFN-gamma production.				
Protease (45–54)	Pol (125–134)	KMIGGIGGFI	HIV-1 infection	human (A2 supertype)	Propato2001
	• Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This epitope can bind three of the five HLA-A2 supertypes alleles (A*0201, A*020 2, A*0203, A*0206 and A*6802)				
Protease (75–84)	Protease (75–84 MN)	VLVGPTPVNI	in vitro stimulation	human (A*0201)	Konya1997
	• Peptide predicted to be reactive based on HLA-A*0201 binding motif • Peptide could stimulate CTL in PBMC from 5/6 seronegative donors • Peptide located in a highly conserved region of protease • Both 9-mer and 10-mer could stimulate CTL: VLVGPTPVNI and LVGPTPVNI • Binding affinity to A*0201 was measured, $C\_1/2\max\mu M = 6$ for 10-mer, 3 for 9-mer • MAL variant of Pr(75-84 MN), with substitutions V77, G78, and P79, gave reduced binding and CTL recognition				
Protease (76–84)	Pol (163–)	LVGPTPVNI	HIV-1 infection	human (A*0201)	Altfeld2001c
	• Epitope name: Pol-163 • HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested • Three additional previously described HLA-A2 epitopes were added to the set of 20, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acute infected individuals recognized at least 1 (median of 1 and maximum of 2) • LVGPTPVNI binds to 4/5 HLA-A2 supertype alleles: A*0201, A*0202, A*0206 (highest affinity) and A*6802, but not A*0203 • 1/22 individuals with chronic HIV-1 infection recognized this epitope by ELISPOT • 0/12 acutely infected individuals recognized this epitope				
Protease (76–84)	Pol (156–164)	LVGPTPVNI	HIV-1 infection	human (A2 supertype)	Propato2001
	• Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus • This epitope can bind three of the five HLA-A2 supertypes alleles (A*0201, A*020 2, A*0203, A*0206 and A*6802)				

II-B-9 Protease-RT CTL Epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Protease-RT (95–5)	Gag (175–184)	CTLNFPISPI	HIV-1 infection	human (A2 supertype)	Propato2001
	• The epitope starts in Protease and ends in RT • Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus • This epitope can bind all five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802)				
Protease-RT (96–5)	Pol (176–184)	TLNFPISPI	HIV-1 infection	human (A2 supertype)	Propato2001
	• Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus • This epitope can bind three of the five HLA-A2 supertypes alleles (A*0201, A*020 2, A*0203, A*0206 and A*6802)				

II-B-10 RT CTL Epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (3–12)	RT (LAI)	SPIETVPVKL	HIV-1 infection	human (A2, B61)	vanderBurg1997
	• Recognized by CTL from a long-term survivor, EILKEPVGHGV was also recognized • Highly conserved across clades				
RT (3–12)	Pol	SPIETVPVKL		human (B7)	De Groot2001
	• The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes • A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes could stimulate IFNγ production in an ELISPOT assay • SPIETVPVKL was newly identified as HLA-B7 epitope in this study, it had been previously shown to be presented by HLA-A2 and B61				
RT (5–29)	RT (160–184 HXB2)	IETVPVKLKPGMDGPKVKQ-WPLTEE	HIV-1 infection	human (B8)	Walker1989
	• One of five epitopes defined for RT-specific CTL clones in this study				
RT (18–26)	RT (185–193 LAI)	GPKVKQWPL		human (B*0801)	Brander2001
	• C. Brander notes this is a B*0801 epitope				
RT (18–26)	RT (18–26)	GPKVKQWPL	HIV-1 infection	human (B8)	Meier1995, Menendez-Arias1998
	• HIV proteins with mutations in this epitope allowed transactive inhibition of specific CTL-mediated lysis • Article reviewed in [Menendez-Arias1998], with a discussion of antagonism				
RT (18–26)	RT (173–181)	GPKVKQWPL		human (B8)	Goulder1997g, Menendez-Arias1998
	• Included in a study of the B8 binding motif • Article reviewed in [Menendez-Arias1998], with a discussion of antagonism				
RT (18–26)	RT (185–193 LAI)	GPKVKQWPL		human (B8)	Sutton1993
	• Predicted epitope based on B8-binding motifs, from larger peptide IETVPVKLKPGMDGPKVKQWPLTEE				
RT (18–26)	RT (185–193 LAI)	GPKVKQWPL	HIV-1 infection	human (B8)	Klenerman1995, Menendez-Arias1998
	• Naturally occurring antagonist GPRVKQWPL found in viral PBMC DNA and RNA • Article reviewed in [Menendez-Arias1998] with a discussion of antagonism				
RT (18–26)	RT (18–26)	GPKVKQWPL	in vitro stimulation	human (B8)	Zarling1999
	• This study compares the ability of macrophages and dendritic cells to stimulate primary responses in CD8+ lymphocytes isolated from HLA-appropriate HIV-uninfected donors using peptide-pulsed APC – the dendritic cells performed better as APC for the stimulation of primary responses • Strong CTL responses were elicited by the epitopes DRFYKTLRA and GEIYKRWII when presented by either immature or mature dendritic cells – macrophages were not able to prime a CTL response against DRFYKTLRA • A weak response to KLTPLCVSL was stimulated using macrophages as the APC • No detectable response was observed for the following previously-defined HIV epitopes: KIRLRPGGK, ILKEPVHGV, IRLRPGGK, GPKVKQWPL				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (18–26)	RT (185–193)	GPKVKQWPL	HIV-1 infection	human (B8)	Oxenius2000
	• Epitope name: GPK • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable • Two of the 7/8 study subjects that were HLA B8+ recognized this epitope • Patient SC2 (HLA A1, B7/8, Cw0701/0702, DR4/53, DQ7) had CTL responsiveness against epitopes FLKEKGGL, GPKVKQWPL, and GEIYKRWII peptides – FLKEKGGL tetramer staining steadily declined and at day 1340 the FLKEKGGL stained cells were no longer detected and the escape mutant FLKENGGI was found in 8/10 clones • Patient SC11(HLA A1, B8, Cw0201, DR3/11, DR52, DQ2/7) started therapy early, remained on therapy for 40 days, then reinitiated HAART at day 640 had a CTL response to FLKEKGGL, GPKVKQWPL, and GEIYKRWII throughout and received a benefit from the early limited course therapy			
RT (18–26)	Pol	GPKVKQWPL	HIV-1 infection	human (B8)	Seth2001
	• CTL responses were studied by tetramer staining in 41 patients with combination therapy – activated CD8+ T-cells decline as the viral load drops in response to therapy, but the overall level of antigen-specific cells capable of differentiating into effectors stays constant and new epitopes may be recognized				
RT (18–26)	RT (185–193 SF2)	GPKVKQWPL	HIV-1 infection	human (B8)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-B8+ individuals that had a CTL response to this epitope broken down by group: 0/3 group 1, 0/3 group 2, and 2/2 group 3				
RT (18–26)	Pol (171–180)	GPKVKQWPL	HIV-1 infection, HIV-1 exposed seronegative	human (B8)	Kaul2001a
	• GPKVKQWPL is cross-reactive for clades A, B, C, and D • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers				
RT (18–26)	RT (18–26)	GPKVKQWPL	HIV-1 infection	human (B8)	Day2001
	• B8-restricted CTL accounted for about 1/3 of the total CTL response in one individual				
RT (18–26)	RT	GPKVKQWPL	HIV-1 infection	human (B8)	Oxenius2002b
	• Epitope name: GPK • Using previously defined epitopes [Oxenius2000, Oxenius2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI). • STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.				
RT (18–27)	Pol	GPKVKQWPLT		human (B7, B8)	De Groot2001
	• The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes were identified that could stimulate IFNγ production in an ELISPOT assay • GPKVKQWPLT was confirmed as a previously identified HLA-B8 epitope, and newly identified as an HLA-B7 epitope in this study				
RT (33–41)	RT (33–41 LAI)	ALVEICTEM	HIV-1 infection	human (A*0201)	Brander2001
	• C. Brander notes this is an A*0201 epitope				
RT (33–41)	RT (33–41 LAI)	ALVEICTEL	HIV-1 infection	human (A*0201)	Samri2000
	• This epitope contains the mutation M41L, a mutation induced by nucleosidee reverse transcriptase inhibitors • Patient 201#5, (A*0201), was found by ELISPOT to recognize the mutated peptide after zidovudine treatment, but not the wild-type peptide – the mutation M41L gave an increased A2 binding score (http://bimas.dcrt.nih.gov/molbio/hla_bind) compared to the wildtype RT sequence • Three additional A*0201 individuals and one B27 individual did not respond to this epitope before or after treatment • M41L occurred at anchor positions p2 and p9 in several computer predicted RT epitopes (33-41, 32-41, and 40-49) (http//bimas.dcrt.nih.gov/molbio/hla_bind), and increased the predicted binding affinity for 6 HLA molecules (B2705, B5102, C3, A0201, B2705 and B3901)				
RT (33–41)	RT (33–41)	ALVEICTEM	HIV-1 infection	human (A2)	Haas1998
	• Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively) • New clusters of epitopes were defined utilizing different HLA molecules				
RT (33–41)	RT (33–41)	ALVEICTEM	HIV-1 infection	human (A2)	Day2001
	• The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person • SLYNTVATL was the dominant A2 epitope recognized in patients with chronic infection, except for Subject 11841 who recognized 5/8 epitopes and who had a dominant A-2 response to ALVEICTEM				
RT (33–43)	RT (33–43)	ALVEICTEMEK	HIV-1 infection	human (A*0301)	Haas1998
	• Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively) • New clusters of epitopes were defined utilizing different HLA molecules • C. Brander notes that this is an A*0301 epitope in the 1999 database, G. Haas pers. comm.				
RT (33–43)	RT (33–43)	ALVEICTEMEK	HIV-1 infection	human (A*0301)	Brander2001
	• C. Brander notes this is an A*0301 epitope				
RT (33–43)	RT (33–43)	ALVEICTEMEK	HIV-1 infection	human (A3)	Day2001
	• The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person • All patients recognized at least 1 A3 epitope, up to 8 A3 epitopes, but none was clearly dominant				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (38–52)	RT (203–209)	CTEMEKEGKISKIGP	Vaccine	murine (H-2^d)	Burnett2000
	Vaccine *Vector/Type:* Salmonella *HIV component:* RT epitope • A live attenuated bacterial vaccine, Salmonella SL3261-pHART, with an inserted HIV epitope in the Lpp-OmpA-HIV fusion protein, induced a specific CTL response in BALB/c mice (<15% lysis assayed by Cr-release of target cells)				
RT (38–52)	RT (205–219 BRU)	CTEMEKEGKISKIGP	Vaccine	murine (H2^k)	De Groot1991, Menendez-Arias1998
	Vaccine *Vector/Type:* recombinant protein *Strain:* BRU *HIV component:* RT • Murine and human helper and CTL epitope. • Epitope noted in a review by [Menendez-Arias1998] to be located in the "fingers" domain of RT and is a helper and CTL epitope.				
RT (38–52)	RT (205–219)	CTEMEKEGKISKIGP	HIV-1 infection	human (broad)	Hosmalin1990, Menendez-Arias1998
	• Murine and human helper and CTL epitope. • Epitope noted in a review by [Menendez-Arias1998] to be located in the "fingers" domain of RT and is a helper and CTL epitope.				
RT (39–47)	RT (206–214)	TEMEAEGKI	in vitro stimulation	C3H/HeJ mice	Leggatt1997
	• Ala-substituted nonamer-peptide used to test a non-radioactive assay for murine CTL recognition of peptide-MHC class I complexes • The new assay is CTL adherence assay (CAA), and is based on the discovery that CTL develop adhesive properties upon TCR triggering • Substitutions in TEMEAEGKI that reduce cytolytic activity were correctly detected by CAA				
RT (39–47)	RT	TEMEKEGKI		murine (H-2K^k)	Leggatt1998
	• Epitope variants were examined for CTL response in concert with H-2K^k MHC class I binding – all of the following combinations were observed: (i) two single mutations which did not alone abrogated CTL activity did abrogate activity when combined, (ii) loss of recognition of a single substitution could be restored by an additional substitution, and (iii) sometimes there was recognition of two single substitutions as well as the combination of those substitutions • 2E and 9I are anchor residues for H-2K^k – if you have M in the third position, it enhances H-2K^k binding 10-fold, but polymorphism at this site is important for the overall conformation of the peptide and can influence T cell recognition				
RT (42–50)	RT (42–50 LAI)	EKEGKISKI	HIV-1 infection	human (B*5101)	Brander2001
	• C. Brander notes this is a B*5101 epitope				
RT (42–50)	RT (42–50 LAI)	EKEGKISKI	HIV-1 infection	human (B51)	Haas1998
	• Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively) • New clusters of epitopes were defined utilizing different HLA molecules				
RT (57–65)	Pol (236–244)	NTPVFAIKK	HIV-1 infection	human (A3 supertype)	Propato2001
	• Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus • This epitope can bind 3/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801)				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (73–82)	RT (73–82 LAI)	KLVDFRELNK	HIV-1 infection	human (A3)	Samri2000
	• This epitope contains the mutation L74V, a frequent mutation induced by nucleoside reverse transcriptase inhibitors • The wild-type, but not the mutated peptide, was recognized before and after zidovudine treatment in A3-restricted patients 252#0 and 252#4 • Mutation L74V affects the p2 anchor position in RT epitopes and was predicted to reduce binding to A3 (http://bimas.dcrt.nih.gov/molbio/hla_bind)				
RT (73–82)	RT (228–237)	KLVDFRELNK	HIV-1 infection	human (A3)	Yu2002a
	• Epitope name: A3-KK10 • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 0/14 HLA-A3 positive individuals had detectable A3-restricted responses to this epitope during acute infection, but only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 3/7 individuals began to have detectable responses to this epitope after STI.				
RT (93–101)	(LAI)	GIPHPAGLK		(A3)	Altfeld2000a, Brander2001
RT (93–101)	RT (248–257)	GIPHPAGLK	HIV-1 infection	human (A3)	Yu2002a
	• Epitope name: A3-GK9 • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 0/14 HLA-A3 positive individuals had detectable A3-restricted responses to this epitope during acute infection, but only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 1/7 individuals began to have detectable responses to this epitope after STI.				
RT (93–102)	Pol (240–249 93TH253 subtype CRF01)	GIPHPAGLKK	HIV-1 exposed seronegative	human (A11)	Sriwanthana2001
	• Epitope name: P248-257 • This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand • HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed • This epitope was weakly reactive in the HEPS study subject 265 who was HLA A2/A11 and after a second stimulation *in vitro* gave a strong response in HEPS study subject 128 who was HLA A11/A33				
RT (93–102)	Pol (240–249 93TH253 subtype CRF01)	GIPHPAGLKK	HIV-1 infection	human (A11)	Bond2001
	• HLA-A11 CRF01 (called subtype E in Bond et al.) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive • 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 finding and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified • This is one of the new A11 epitopes identified through the streamlined EpiMatrix method, and 2/8 tested FSWs recognized it • This epitope was highly conserved in other subtypes, and exact matches were common				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (98–113)	Pol (254–264 BH10, LAI)	AGLKKKKSVTVLDVGD	HIV-1 infection	human	Maksiutov2002
	• This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins. • This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is GLKKKKSVTVL) has similarity with the CD166 antigen (activated leukocyte-cell adhesion molecule), fragment GLKKRESLTLI.				
RT (98–113)	RT (252–266)	AGLKKKKSVTVLDVGD	HIV-1 infection	human (Cw4)	Bernard1998
	• This study focuses on six rare long-term survivor HIV-infected people who were infected for many years without exhibiting immune dysregulation – such immunologically normal HIV-infected (INHI) cases occur at a frequency between 0.1 and 1% in the infected population • No direct CTL were found in any of the six INHIs, but above background CTLp activity was founded in 3/6 INHIs				
RT (103–117)	RT (257–251)	KKSVTVLDVGDAYFS	HIV-1 infection	human (Cw4)	Bernard1998
	• This study focuses on six rare long-term survivor HIV-infected people who were infected for many years without exhibiting immune • No direct CTL were found in any of the six INHIs, but above background CTLp activity was founded in 3/6 INHIs				
RT (107–115)	RT (262–270 IIIB)	TVLDVGDAY		(B*3501)	Brander2001
	• C. Brander notes this is a B*3501 epitope				
RT (107–115)	RT (262–270 IIIB)	TVLDVGDAY	HIV-1 infection	human (B35)	Menendez-Arias1998, Wilson1996
	• Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study • TVLDMGDAC is a naturally occurring variant that is less reactive • [Menendez-Arias1998], in a review, notes that this epitope includes a catalytic residue (Asp-110) in the active site of RT				
RT (107–115)	Pol (262–270 IIIB)	TVLDVGDAY	HIV-1 infection	human (B35)	Wilson1999a
	• This study describes maternal CTL responses in the context of mother-to-infant transmission • Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants • An additional variant that gave a positive CTL response: TVLDMGDAC				
RT (107–115)	Pol (262–270)	TVLDVGDAY	HIV-1 infection	human (B35)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
RT (107–115)	RT (262–270 SF2)	TVLDVGDAY	HIV-1 infection	human (B35)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-B35+ individuals that had a CTL response to this epitope broken down by group: 1/2 group 1, 0/2 group 2, and 0/1 group 3				
RT (107–115)		TVLDVGDAY	HIV-1 infection	human (B35)	Sabbaj2002b
	• Epitope name: Pol-TY9				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Among HIV+ individuals who carried HLA B35, 8/21 (38%) recognized this epitope				
RT (107–115)	Pol	TVLDVGDAY	HIV-1 infection	human (B35)	Sabbaj2002a
	• IFNgamma T-cell responses in breast milk of 5 HIV-1 infected women from the US and 6 from Zambia were tested with using Elispot. 11/11 women responded to Gag, 8/11 responded to Pol, 7/11 women to Nef, and 2/5 women to Env peptide pools. These responses were shown to be primarily due to CD8+ T-cells in one woman, and another woman had cytolytic responses measured by Cr-release. • T-cells in breast milk from a volunteer who was HLA A3, A11, B35, B51 induced IFNgamma after stimulation with either of two overlapping peptides that carry known B35 epitope TVLDVGDAY. • The frequencies of responses in the two compartments differed, and 2/4 women that responded to epitopes in Nef 101-205 and Pol 601-710 showed responses in breast milk but no detectable responses in peripheral blood cells.				
RT (108–118)	RT (267–277)	VLDVGDAYFSV	in vitro stimulation	human (A*0201)	vanderBurg1996
	• High dissociation rate, but immunogenic in primary CTL induction after repeated stimulations with peptide • CTL generated by in vitro stimulation of PBMC derived from uninfected individual				
RT (108–118)	RT (267–277)	VLDVGDAYFSV	HIV-1 infection	human (A2)	Kundu1998b
	• Allogeneic dendritic cells (DCs) were obtained from HLA-identical siblings, pulsed with rgp160 MN or A2-restricted HIV-1 epitope peptides, and infused monthly into six HIV-infected patients • 1/6 showed increased env-specific CTL and increased lymphoproliferative responses, 2/6 showed increase only in proliferative responses, and 3/6 showed no change – pulsed DCs were well tolerated • VLDVGDAYFSV is a conserved HLA-A2 epitope included in this study – 4/6 patients had this sequence as their HIV direct sequence, but only one of these had a detectable CTL response – the other two had the sequences EEDVGDAYFSV and ELDVGDAYFSV and no detectable CTL response				
RT (108–118)	RT (267–277)	VLDVGDAYFSV	in vitro stimulation	human (A2)	vanderBurg1995
	• Binds HLA-A*0201 – CTL generated by in vitro stimulation of PBMC from an HIV negative donor • VLDVGDAYFSV is in a functional domain				
RT (108–118)	Pol (263–273)	VLDVGDAYFSV	HIV-1 infection	human (A2, A*0201)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
RT (108–122)	RT (257–251)	VLDVGDAYFSVPLDE	HIV-1 infection	human (Cw4)	Bernard1998
	• This study focuses on six rare long-term survivor HIV-infected people who were infected for many years without exhibiting immune dysregulation – such immunologically normal HIV-infected (INHI) cases occur at a frequency between 0.1 and 1% in the infected population • No direct CTL were found in any of the six INHIs, but above background CTLp activity was founded in 3/6 INHIs				
RT (113–120)	Pol (268–275 SF2)	DAYFSVPL	HIV-1 infection	human (B*5101, B24)	Tomiyama1999
	• HLA-B27, -B51, and -B57 are associated with slow progression to AIDS, while HLA -B35, -B8, -B24 are associated with a rapid progression to AIDS (Nat. Med. 2:405, 1996;Lancet 22:1187, 1986;Hum Immunol 22:73, 1988;Hum Immunol 44:156, 1995) • 15% of Japanese populations carry HLA-B51 while HLA-B27 and -B57 are detected in less than 0.3% • Of the 172 HIV-1 peptides with HLA-B*5101 anchor residues, 33 bound to HLA-B*5101, seven of these peptides were reactive with CTL from 3 B*5101 positive individuals, and six were properly processed • Four of the six epitopes were highly conserved among B subtype sequences, DAYFSVPL is conserved				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (116–135)	Pol (271–290)	FSVPLDEDFRKYTAFTIPSI	HIV-1 infection	human	Novitsky2002
	• HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
RT (117–126)	Pol (264–273 93TH253 subtype CRF01)	SVPLDESFRK	HIV-1 exposed seronegative	human (A11)	Sriwanthana2001
	• Epitope name: P272-281 • This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand • HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed • This epitope after a second stimulation *in vitro* gave a strong response in HEPS study subject 128 who was HLA A11/A33				
RT (117–126)	Pol (264–273 93TH253 subtype CRF01)	SVPLDESFRK	HIV-1 infection	human (A11)	Bond2001
	• HLA-A11 CRF01 (called subtype E in Bond et al.) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive • 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 finding and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified • This is one of the new A11 epitopes identified through the streamlined EpiMatrix method, and 3/8 tested FSWs recognized it • This epitope was only conserved in CRF01, and subtype A and B, and exact matches were uncommon				
RT (118–127)	RT (273–282 SF2)	VPLDKDFRKY	HIV-1 infection	human (B*3501)	Menendez-Arias1998, Tomiyama1997
	• A CTL clone responsive to this epitope was obtained • 4/7 B35-positive individuals had a CTL response to this epitope • A K to E substitution at position 5 abrogates specific lysis, and reduces binding to B*3501 • [Menendez-Arias1998], in a review, notes that a Glu to Lys (E to K) change abrogates CTL activity, but that both VPLDEDFRKY and VPLDKDFRKY can serve as HLA-B35 epitopes, so the change must alter T cell receptor binding – residues in this epitope may be important for polymerase activity				
RT (118–127)	RT (273–282 IIIB)	VPLDEDFRKY	HIV-1 infection	human (B*3501)	Brander2001
	• C. Brander notes this is a B*3501 epitope				
RT (118–127)	Pol (273–282)	VPLDKDFRKY	HIV-1 infection	human (B*3501)	Tomiyama2000a
	• CD8+ T-cells that bound one of six HIV-specific B*3501-epitope tetramers did not express CD28 or CD45A • A significant increase in CD28-CD45RA- cells and a decrease of CD28+CD45RA+ cells was observed in chronically HIV-1-infected individuals relative to healthy individuals • CD28-CD45RA- cells are likely to be effector cells and have high levels of perforin in their cytoplasm • The mean percentage of total CD28- CD8+ cells in chronically infected HIV-1-infected patients was 76.6% in comparison to HIV-1-uninfected individuals (40.6%)				
RT (118–127)	(SF2)	VPLDEDFRKY	HIV-1 infection	human (B*3501)	Tomiyama2000b
	• Epitope name: HIV-B3501-SF2-4				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• B*3501 VPLDEDFRKY tetramer binding did not inhibit CTL activity of a clone that react with both HLA-B*3501 than HLA-B*5101 presentation of the epitope IPLTEEAEL				
RT (118–127)	RT (273–282 IIIB) • Binds HLA-B*3501	VPLDEDFRKY	HIV-1 infection	human (B*3501, B35)	Shiga1996
RT (118–127)	(SF2) • HLA B35 is associated with rapid disease progression • The sequences of 9 previously described HIV-1 B35 CTL epitopes were obtained in 10 HLA B35+ and 19 HLA B35- individuals • 3/9 CTL epitopes had substitutions that were more common in B35+ individuals than in B35- individuals – only one of these reduced the binding of the peptide to B35 and was shown to be an escape mutation • ——E—- was found in 8/10 of the B35+ individuals, and three of the B35- individuals – the D –> E substituted peptide had similar binding affinity to B35 and was equally susceptible to a CTL clone	VPLDKDFRKY	HIV-1 infection	human (B35)	Kawana1999
RT (118–127)	RT (273–282 IIIB) • HIV IIIB proteins were used to define the range of CTL epitopes recognized by three lab workers accidentally infected with HIV-1 IIIB • VPLDKDFRKY, a variant found in HIV MN, was not recognized • VPHDEDFRKY, a variant found in HIV YU2, was not recognized • This epitope was type-specific and conserved in only one other B subtype sequence	VPLDEDFRKY	HIV-1 infection	human (B35)	Sipsas1997
RT (118–127)	RT (273–282 SF2) • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-B35+ individuals that had a CTL response to this epitope broken down by group: 1/2 group 1, 0/2 group 2, and 1/1 group 3	VPLDEDFRKY	HIV-1 infection	human (B35)	Altfeld2001b
RT (118–127)	• Epitope name: Pol-VY10 • Among HIV+ individuals who carried HLA B35, 5/21 (24%) recognized this epitope	VPLDEDFRKY	HIV-1 infection	human (B35)	Sabbaj2002b
RT (126–135)	RT (293–302 HXB) • A novel CTL clone was defined with a panel of recombinant vaccinia-RT-infected B-LCL target cells using PBMCs donated by a patient who was HIV-seropositive for 6 years and had not received any antiretroviral therapy • There is evidence that some CTL epitopes are poorly presented on the surface of infected cells, but this RT epitope was recognized as effectively on HIV-infected cells as on peptide-pulsed targets	KYTAFTIPSI	HIV-1 infection	human (A2)	Shankar1998
RT (127–135)	Pol (316–) • Epitope name: Pol-316 • HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested	YTAFTIPSI	HIV-1 infection	human (A2)	Altfeld2001c

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Three additional previously described HLA-A2 epitopes were added to the set of 20, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acute infected individuals recognized at least 1 (median of 1 and maximum of 2) • 2/22 individuals with chronic HIV-1 infection recognized this epitope in ELISPOT • 0/12 acutely infected individuals recognized this epitope • YTAFTIPSI binds to five HLA-A2 supertype alleles: A*0201, A*0202,A*0203, A*0206 and A*6802 (highest affinity)				
RT (127–135)	Pol (306–314)	YTAFTIPSI	HIV-1 infection	human (A2 supertype)	Propato2001
	• Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus • This epitope can bind all five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802)				
RT (128–135)		TAFTIPSI	HIV-1 infection	human (A*0217, B*5101)	Sabbaj2002b
	• Epitope name: Pol-TI8 • This study monitored epitope responses in HIV-1 infected minority women living in the United States • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release • Patient 01RCH46 was Hispanic, on HAART, and had a viral load of 21000 and CD4 count of 623 – she also recognized GELDRWEKI, p17(11-19), HLA B*4002, and KETINEEAA p24(70-78), HLA B*4002 • Among HIV+ individuals who carried HLA A*02, 7/36 (19%) recognized this epitope, two of which also carried B*5101 which can also restrict this epitope				
RT (128–135)	RT (295–302 IIIB)	TAFTIPSI	HIV-1 infection	human (B*5101)	Brander2001
	• C. Brander notes this is a B*5101 epitope				
RT (128–135)	Pol (283–290 SF2)	TAFTIPSI	HIV-1 infection	human (B*5101)	Tomiyama1999
	• HLA-B27, -B51, and -B57 are associated with slow progression to AIDS, while HLA-B35, -B8, -B24 are associated with a rapid progression to AIDS (Nat. Med. 2:405, 1996;Lancet 22:1187, 1986;Hum Immunol 22:73, 1988;Hum Immunol 44:156, 1995) • 15% of Japanese populations carry HLA-B51 while HLA-B27 and -B57 are detected in less than 0.3% • Of the 172 HIV-1 peptides with HLA-B*5101 anchor residues, 33 bound to HLA-B*5101, seven of these peptides were reactive with CTL from 3 B*5101 positive individuals, and six were properly processed • Four of the six epitopes were highly conserved among B subtype sequences, but TAFTIPSI is somewhat variable				
RT (128–135)	RT (295–302)	TAFTIPSI	HIV-1 infection	human (B*5101)	Samri2000
	• Epitope name: P5 • The epitope TAFTIPSI was recognized by patient 246#1 in a study of the effects of therapy escape mutations on CTL recognition				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (128–135)	RT (128–135 IIIB)	TAFTIPSI	HIV-1 infection	human (B*5101)	Moore2002b
	• HIV polymorphisms in the RT protein were examined relation to HLA alleles found in a population of 473 participants in the Western Australian HIV Cohort Study. 64 significant associations between polymorphisms at particular positions and HLA alleles were detected, for HLA-B7, -B12, -B35 and -B15. Fifteen of these were in positions with known epitopes, 4 in anchor residues, 11 in other positions. Six additional polymorphic sites associated with particular HLA molecules flanked known epitopes and may relate to processing. • TAFTIPSI was one of two epitopes characterized in detail. C-terminal I135x substitutions were associated with people who carried HLA-B5 – 39/40 (98%) of HLA-B*5101 individuals had substitutions in this position, while only 127/431 (29%) who did not have HLA-B*5101 did. The predominant substitution was kytaftipsT, and this mutation is predicted to abrogate binding to HLA-B*5101.				
RT (128–135)	RT (295–302 IIIB)	TAFTIPSI	HIV-1 infection	human (B51)	Menendez-Arias1998, Sipsas1997
	• HIV IIIB proteins were used to define the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB • TAFTIPST, a variant found in HIV-1 CAM1, was also recognized but 100-fold more peptide was needed • TAFTIPSV, a variant found in HIV-1 VE1RT, was also recognized, but 10-fold more peptide was needed • TVFTIPSI, a variant found in HIV-1 MANC, was also recognized • [Menendez-Arias1998], in a review, notes that this epitope includes a region near the active site of RT – the substitution of the position two conservative change from A to V decreases CTL recognition				
RT (128–135)	RT (295–302)	TAFTIPSI	HIV-1 infection	human (B51)	Betts2000
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes • Three of the four individuals that responded to SLYNTVATL recognized additional HIV epitopes, and all three were also HLA B51 and recognized this epitope as well as other epitopes				
RT (128–135)	RT (295–302)	TAFTIPSI	HIV-1 infection	human (B51)	Oxenius2000
	• Epitope name: TAF • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable • None of the 8 study subjects recognized this epitope but none were HLA B51+				
RT (128–135)	RT (295–302 LAI)	TAFTIPSI	HIV-1 infection	human (B51)	Mollet2000
	• Epitope name: P5 • A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses • In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished • Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (128–135)	Pol	TAFTIPSI	HIV-1 infection	human (B51)	Sabbaj2002a
	• IFNgamma T-cell responses in breast milk of 5 HIV-1 infected women from the US and 6 from Zambia were tested with using Elispot. 11/11 women responded to Gag, 8/11 responded to Pol, 7/11 women to Nef, and 2/5 women to Env peptide pools. These responses were shown to be primarily due to CD8+ T-cells in one woman, and another woman had cytolytic responses measured by Cr-release. • T-cells in breast milk from a volunteer who was HLA A3, A11, B35, B51 induced IFNgamma after stimulation with either of two overlapping peptides that carry known B51 epitope TAFTIPSI. • The frequencies of responses in the two compartments differed, and 2/4 women that responded to epitopes in Nef 101-205 and Pol 601-710 showed responses in breast milk but no detectable responses in peripheral blood cells.				
RT (151–159)	Pol (306–314 SF2)	QGWKGSPAI	HIV-1 infection	human (B*5101)	Tomiyama1999
	• HLA-B27, -B51, and -B57 are associated with slow progression to AIDS • 15% of Japanese populations carry HLA-B51 while HLA-B27 and -B57 are detected in less than 0.3% • Of the 172 HIV-1 peptides with HLA-B*5101 anchor residues, 33 bound to HLA-B*5101, seven of these peptides were reactive with CTL from 3 B*5101 positive individuals, and six were properly processed • Four of the six epitopes were highly conserved among B subtype sequences, QGWKGSPAI is conserved				
RT (153–165)	RT (308–320)	WKGSPAIFQSSMT	HIV-1 infection	human (B7)	Brander1995b
	• Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study				
RT (153–165)	Pol (308–320)	WKGPAIFQSSMT	HIV-1 infection	human (B7)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
RT (153–167)	RT (SF2)	WKGSPAIFQSSMTKI	HIV-1 infection	human	Altfeld2001a
	• HIV+ individual AC-06 was tested for reactive overlapping peptides spanning all HIV-1 proteins in an ELISPOT and was found to react with 12 peptides from 7 proteins, suggesting that the breadth of CTL responses are underestimated if accessory proteins are not included in the study • RT peptides SQIYPGIKVRQLCKL and WKGSPAIFQSSMTKI were recognized				
RT (156–164)	RT (311–319 SF2)	SPAIFQSSM	HIV-1 infection	human (B*3501)	Menendez-Arias1998, Tomiyama1997
	• A CTL clone responsive to this epitope was obtained • Only 1/7 B35-positive individuals had a CTL response to this epitope • [Menendez-Arias1998], in a review, notes that this epitope is near the active site of RT				
RT (156–164)	RT (311–319 SF2)	SPAIFQSSM	HIV-1 infection	human (B35)	Menendez-Arias1998, Shiga1996
	• Binds HLA-B*3501 • [Menendez-Arias1998], in a review, notes that this epitope includes catalytic residues in the active site of RT				
RT (156–164)	Pol (311–319)	SPAIFQSSM	HIV-1 infection	human (B35)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
RT (156–164)	Pol (156–164 HXB2)	SPAIFQSSM	HIV-1 infection	human (B7)	Hay1999b
	• CTL response to IPRRIRQGL was the immunodominant response in a rapid progressor – there was a subdominant response to SPAIFQSSM in Pol, and interestingly, no response to commonly immunodominant HLA A*0201 epitope SLYNTVATL, although this individual was HLA A*0201				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The individual showed a strong initial CTL response at the time of the initial drop in viremia, but it was quickly lost, although memory cells persisted • Despite the initial narrow response to two epitopes, no other CTL responses developed • No HIV-specific lymphoproliferative responses were detected in this patient, and neutralizing antibody response was weak • Variants of this epitopes were observed in vivo (spaifqCsm, spSifqssm), but the binding motifs for B7 were preserved (P2, and C-term aromatic or hydrophobic)				
RT (156–164)	Pol	SPAIFQSSM	HIV-1 infection	human (B7)	Islam2001
	• Subject 053i was followed longitudinally from acute infection through death, and had rapid progression to AIDS • This individual had a dominant response to IPRRIRQGL with strong in vivo activated responses and in vitro stimulated memory responses and a subdominant response to SPAIFQSSM – during the course of disease progression (4 Years), the functional CTL responses were lost and no sequence variation occurred with in both epitopes, but CTL clones specific for IPRRIRQGL persisted throughout				
RT (156–164)	RT (323–331 SF2)	SPAIFQSSM	HIV-1 infection	human (B7)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-B7+ individuals that had a CTL response to this epitope broken down by group: 0/4 group 1, 0/3 group 2, and 1/1 group 3				
RT (156–164)	RT (156–164)	SPAIFQSSM	HIV-1 infection	human (B7)	Yu2002a
	• Epitope name: B7-SM9 • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 1/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. 3/4 individuals had detectable responses to this epitope after STI.				
RT (156–165)	RT (311–319 LAI)	SPAIFQSSMT	HIV-1 infection	human (B35)	Samri2000
	• Epitope name: P4 • This epitope contains the mutation P157S which can be induced by nucleosidee reverse transcriptase inhibitors • It was recognized by patient 252#0 in a study of the effects of therapy escape mutations on CTL recognition				
RT (156–165)	RT (311–319 SF2)	SPAIFQSSMT		human (B7)	Brander1997, Menendez-Arias1998
	• Pers. Comm. from C. Hey and D. Ruhl to C. Brander and B. Walker • [Menendez-Arias1998], in a review, notes that this epitope includes catalytic residues in the active site of RT				
RT (156–165)	RT (311–319 SF2)	SPAIFQSSMT	HIV-1 infection	human (B7)	Mollet2000
	• Epitope name: P4 • A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished • Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change				
RT (156–165)	Pol	SPAIFQSSMT		human (B7)	De Groot2001
	• The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes • A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes could stimulate IFNγ production in an ELISPOT assay • SPAIFQSSMT was confirmed as a previously identified HLA-B7 epitope in this study				
RT (156–165)	RT (IIIB)	SPAIFQSSMT	HIV-1 infection	human (B7)	Moore2002b
	• HIV polymorphisms in the RT protein were examined relation to HLA alleles found in a population of 473 participants in the Western Australian HIV Cohort Study. 64 significant associations between polymorphisms at particular positions and HLA alleles were detected, for HLA-B7, -B12, -B35 and -B15. Fifteen of these were in positions with known epitopes, 4 in anchor residues, 11 in other positions. Six additional polymorphic sites associated with particular HLA molecules flanked known epitopes and may relate to processing. • HLA-B7+ individuals with a S162x (18/33) substitution had higher viral loads than those that did not, suggesting escape was associated with diminished immune control of viremia.				
RT (158–166)	RT (325–333 LAI)	AIFQSSMTK	HIV-1 infection	human (A*0301)	Brander2001
	• C. Brander notes this is an A*0301 epitope				
RT (158–166)	Pol	AIFQSSMTK	HIV-1 infection, Vaccine	human, macaque (A*0301, A11, A33)	Hanke2000, Wee2002
	Vaccine *Vector/Type:* DNA prime with vaccinia MVA boost *Strain:* subtype A *HIV component:* p17, p24, polyepitope • The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000]. • Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].				
RT (158–166)	RT (325–333 LAI)	AIFQSSMTK	HIV-1 infection	human (A*1101)	Brander2001
	• C. Brander notes this is an A*1101 epitope				
RT (158–166)	Pol (313–321)	AIFQSSMTK	HIV-1 infection	human (A*1101)	Fukada2002
	• Counterparts for eight known clade B HLA A*1101 epitopes were generated for clade E (CRF01). Three epitopes, identical among clade A-E, were cross-reactive and recognized by clade E infected individuals. The clade E and B analogs to three more HLA A*1101 epitopes was recognized in a clade specific manner. Two other HLA A*1101 clade B defined epitopes were found not to have stimulated a response in clade E infected individuals. • AIFQSSMTK is commonly found in viruses representing subtypes A-E. It was strongly recognized by CTL from 2/5 B clade infected Japanese subjects, and 5/6 E clade infected Thai subjects.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (158–166)	RT (325–333)	AIFQSSMTK	HIV-1 infection	human (A*1101, A3, A*0301, A*6801)	Menendez-Arias1998, Threlkeld1997
	• Study of the fine specificity of an A3-like super-type epitope (the A3 super-type includes A*0301, A*1101, A*3101, A*3301, and A*6801) • A3 super-type is characterized by a hydrophobic or hydroxyl containing anchor residue at position 2, and a positive charge in the C-term position • While most lines were specific, promiscuous cloned CTL lines were also derived from HIV+ donors that could recognize epitope presented by either A3 or A11 or A*6801 • Alanine substitutions throughout the epitope and natural variants indicate that the same amino acid positions are critical for presentation by either MHC molecule, A3 or A11 • AIFQSSMTK is presented by three members of the A3 superfamily: A*0301, A*1101, and A*6801, and the naturally occurring variants A1S and K9R are recognized with similar efficiency to wild type epitope – AIFQRSMTR can also bind to two additional members of the A3 superfamily, A*3101 and A*3301				
RT (158–166)	RT	AIFQSSMTK	HIV-1 infection	human (A11)	Wagner1998a
	• CTL specific for HIV epitopes were used to show that the mediators of both the cytolytic (granzyme A was used as the marker) and non-cytolytic (HIV-1 inhibitory chemokines MIP-1 α and RANTES were used as markers) anti-viral responses are localized within the CTL's cytotoxic granules				
RT (158–166)	RT (325–333 LAI)	AIFQSSMTK	Peptide-HLA interaction	human (A11)	Menendez-Arias1998, Zhang1993
	• Exploration of A11 binding motif, based on Nixon et al. 1991				
RT (158–166)	RT (325–333 LAI)	AIFQSSMTK	HIV-1 infection	human (A11)	McMichael1994
	• Review of HIV CTL epitopes				
RT (158–166)	Pol (305–313 93TH253 subtype CRF01)	AIFQSSMTK	HIV-1 infection, HIV-1 exposed seronegative	human (A11)	Sriwanthana2001
	• Epitope name: P313-321 • This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand • HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed • This epitope was weakly reactive in the HEPS study subject 128 who was HLA A11/A33 • This epitope was strongly reactive in HIV+ study subjects 053 and 184 who carried HLA-A11				
RT (158–166)	Pol (305–313 93TH253 subtype CRF01)	AIFQSSMTK	HIV-1 infection	human (A11)	Bond2001
	• HLA-A11 CRF01 (called subtype E in Bond et al.) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive • 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 finding and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified • This epitope was predicted by the EpiMatrix method to be likely to bind to A11, and it served as an epitope in the FSWs, it was one of the six A11 epitopes that had been previously defined • 6/8 tested FSWs recognized this epitope • An HLA-A11 tetramer was made for this epitope, which was recognized by two subjects – and both subjects had expanded tetramer staining T-cell populations after in vitro stimulation				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This epitope was highly conserved in other subtypes, and exact matches were common				
RT (158–166)	RT (158–166 IIIB)	AIFQSSMTK	HIV-1 infection	human (A11)	Moore2002b
	• HIV polymorphisms in the RT protein were examined relation to HLA alleles found in a population of 473 participants in the Western Australian HIV Cohort Study. 64 significant associations between polymorphisms at particular positions and HLA alleles were detected, for HLA-B7, -B12, -B35 and -B15. Fifteen of these were in positions with known epitopes, 4 in anchor residues, 11 in other positions. Six additional polymorphic sites associated with particular HLA molecules flanked known epitopes and may relate to processing. • HLA-A11+ individuals with a K166x (4/19) substitution had higher viral loads than those that did not, suggesting escape was associated with diminished immune control of viremia.				
RT (158–166)	Pol	SIFQSSMTK	HIV-1 infection	human (A11)	Appay2002
	• Four HIV patients with prolonged clinically successful anti-viral therapy but with ongoing evidence of replication and Nef mRNA transcription, showed specific T-cell responses by Elispot and Tetramer staining, maintained for 2-4 years after initiation of HAART. • Nef epitope recognition was detected in all 4 subjects, gp120, Pol and Gag-specific in 1 or 2 subjects. • The HIV-specific CD8+ T-cells had an intermediate maturation phenotype characterized by low levels of perforin and high levels of CD27 expression.				
RT (158–166)	RT (325–333 IIIB)	AIFQSSMTK	HIV-1 infection	human (A3)	Wilson1996
	• Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study • AIFQSSMTR and AILQSSMTK, naturally occurring variants, were found in infant, and are recognized • TISQSSMTK, a naturally occurring variant, was found in infant and is not recognized				
RT (158–166)	RT (325–333 LAI)	AIFQSSMTK	HIV-1 infection	human (A3)	Cao1997a
	• The consensus peptide of B and D clade viruses is AIFQSSMTK • The consensus peptide of a subset of As is AIFQASMTK and it is less able to stimulate the CTL clone • The consensus peptide of a subset of As is SIFQSSMTK and is as reactive as the originally defined epitope				
RT (158–166)	Pol (325–333 IIIB)	AIFQSSMTK	HIV-1 infection	human (A3)	Wilson1999a
	• This study describes maternal CTL responses in the context of mother-to-infant transmission • Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants • One variant found in an infant gave a positive CTL response: AIFQSSMTR • AIFLSSMTK and TISQSSMTK were escape mutants				
RT (158–166)	RT (325–333 SF2)	AIFQSSMTK	HIV-1 infection	human (A3)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-A3+ individuals that had a CTL response to this epitope broken down by group: 0/7 group 1, 0/4 group 2, and 1/2 group 3				
RT (158–166)	RT (158–166)	AIFQSSMTK	HIV-1 infection	human (A3)	Day2001
	• The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person • All patients recognized at least 1 A3 epitope, up to 8 A3 epitopes, but none was clearly dominant • In two of the subjects, AIFQSSMTK was the dominant epitope				
RT (158–166)	RT Pol (313–321)	AIFQSSMTK	HIV-1 infection	human (A3)	Yu2002a
	• Epitope name: A3-ATK9 • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 0/14 HLA-A3 positive individuals had detectable A3-restricted responses to this epitope during acute infection, but only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 3/7 individuals began to have detectable responses to this epitope after STI.				
RT (158–166)	Pol (337–345)	AIFQSSMTK	HIV-1 infection	human (A3 supertype)	Propato2001
	• Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus • This epitope can bind 3/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801)				
RT (158–166)	Pol (313–321)	AIFQSSMTK	HIV-1 infection	human (A3, A11)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
RT (158–166)	Pol (325–333)	AIFQSSMTK	HIV-1 infection, HIV-1 exposed seronegative	human (A3, A11, A33)	Kaul2001a
	• Variants (S/A)IFQSSMTK are specific for the A/B clades • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure • Among HLA-A3 women, 2/2 HEPS and 3/3 HIV-1 infected women recognized this epitope • The dominant response to this HLA allele was to this epitope in one of the 2/2 HEPS cases and in one of the 3/3 HIV-1 infected women				
RT (158–166)	RT (325–333)	AIFQSSMTK	HIV-1 infection	human (A3.1)	Brander1995b
	• Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study				
RT (158–166)	RT (325–333)	AIFQSSMTK	HIV-1 infection	human (A3.1)	Betts2000
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• 1/11 of the A2+ individuals was HLA A3 and reacted with this epitope as well as two other A3.1 epitopes				
RT (158–166)	RT (325–333 LAI)	AIFQSSMTK		human (A33)	Rowland-Jones1995a
	• Defined as minimal peptide by titration curve, S. Rowland-Jones, Pers. Comm.				
RT (158–166)		AIFQSSMTK	HIV-1 infection	human (A33)	Kaul2001c
	• This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative • The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire • This epitope was recognized in 1/22 HEPS sex worker controls, ML1668				
RT (158–166)	RT (325–333 LAI)	AIFQSSMTK	HIV-1 infection	human (A3supertype)	Mollet2000
	• Epitope name: P3 • A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses • In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished • Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change				
RT (158–166)		AIFQSSMTK	HIV-1 infection	human (B*0301)	Wilson2000a
	• Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load was also found • All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39 • ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK • The subject with A*0201 had a moderatly strong response to SLYNTVATL • Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705 • No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL				
RT (158–182)	RT (325–349 PV22)	AIFQSSMTKILEPFRKQNP-DIVIYQ	HIV-1 infection	human (A11)	Jassoy1993
	• HIV-1 specific CTLs release γ-IFN, and α- and β-TNF				
RT (158–182)	RT (325–349)	AIFQSSMTKILEPFRKQNP-DIVIYQ	HIV-1 infection	human (A11)	Price1995
	• Study of cytokines released by HIV-1 specific activated CTL				
RT (164–172)	Pol (343–351)	MTKILEPFR	HIV-1 infection	human (A3 supertype)	Propato2001
	• Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus • This epitope can bind 4/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801)				
RT (173–181)	RT (173–181 LAI) • C. Brander notes this is an A*3002 epitope	KQNPDIVIY		human (A*3002)	Brander2001, Goulder2001a
RT (173–181)	RT • Epitope name: KY9 (RT-53) • HLA-A*3002 is very common in African populations, 50% of Zimbabweans express HLA-A30, 44% in African Zulu, so five new HIV epitopes were characterized that are presented by this HLA molecule • A rapid method was developed combining ELISPOT with intracellular IFN-γ staining of PBMCs to map optimal epitopes, then HLA presenting molecules were defined – this method was completed within 48 to 72 hours of receipt of blood • Two individuals were studied: Subject 199 (HLA A*0201/*3002 B*4402/51 Cw2/5), a Caucasian, and Subject 6007 (HLA A*3002/ B53/*5801 Cw4/7) an African-Caribbean • In both HLA-A*3002 individuals the response to RSLYNTVATLY was dominant • In subject 199 four additional A*3002 epitopes were identified • Three quantitative assays, ELISPOT, precursor frequency and chromium release, confirmed a hierarchy of response: RY11 (p17) > KY9 (gp41) > KY9 (RT-53) > IY9 (gp41)	KQNPDIVIY	HIV-1 infection	human (A*3002)	Goulder2001a
RT (175–183)	RT (328–336 IIIB) • A CTL clone responsive to this epitope was obtained • 3/7 B35-positive individuals had a CTL response to this epitope • D to E, or V to I, substitutions at positions 3 or 5, respectively, reduces CTL activity and binding to B*3501	NPDIVIYQY	HIV-1 infection	human (B*3501)	Tomiyama1997
RT (175–183)	RT (328–336 IIIB) • C. Brander notes this is a B*3501 epitope	NPDIVIYQY	HIV-1 infection	human (B*3501)	Brander2001
RT (175–183)	RT (342–350 LAI) • C. Brander notes this is a B*3501 epitope	HPDIVIYQY	HIV-1 infection	human (B*3501)	Brander2001
RT (175–183)	Pol (330–338) • CD8+ T-cells that bound one of six HIV-specific B*3501-epitope tetramers did not express CD28 or CD45A • A significant increase in CD28-CD45RA- cells and a decrease of CD28+CD45RA+ cells was observed in chronically HIV-1-infected individuals relative to healthy individuals • CD28-CD45RA- cells are likely to be effector cells and have high levels of perforin in their cytoplasm • The mean percentage of total CD28- CD8+ cells in chronically infected HIV-1-infected patients was 76.6% in comparison to HIV-1-uninfected individuals (40.6%)	NPDIVIYQY	HIV-1 infection	human (B*3501)	Tomiyama2000a
RT (175–183)	RT (175–183 IIIB) • HIV polymorphisms in the RT protein were examined relation to HLA alleles found in a population of 473 participants in the Western Australian HIV Cohort Study. 64 significant associations between polymorphisms at particular positions and HLA alleles were detected, for HLA-B7, -B12, -B35 and -B15. Fifteen of these were in positions with known epitopes, 4 in anchor residues, 11 in other positions. Six additional polymorphic sites associated with particular HLA molecules flanked known epitopes and may relate to processing.	NPDIVIYQY	HIV-1 infection	human (B*3501)	Moore2002b

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• NPDIVIYQY was one of two epitopes characterized in detail. D177x substitutions are know to specifically abrogate binding to HLA-B*3501, and not other B*35 subtypes. D177x substitutions were associated with people who carried HLA-B*3501 and not other B*35 subtypes; considering high resolution typing generally strengthened the B*35 associations.				
RT (175–183)	RT (342–350 LAI)	HPDIVIYQY	HIV-1 infection	human (B35)	McMichael1994
	• Review of HIV CTL epitopes				
RT (175–183)	RT (329–337)	HPDIVIYQY	HIV-1 infection	human (B35)	Rowland-Jones1995b
	• NPDIVIYQY preferred sequence for some CTL clones, HIV-2 NPDVILIQY is also recognized				
RT (175–183)	(SF2)	NPDIVIYQY	HIV-1 infection	human (B35)	Kawana1999
	• HLA B35 is associated with rapid disease progression • The sequences of 9 previously described HIV-1 B35 CTL epitopes were obtained in 10 HLA B35+ and 19 HLA B35- individuals • 3/9 CTL epitopes had substitutions that were more common in B35+ individuals than in B35- individuals – only one of these reduced the binding of the peptide to B35 and was shown to be an escape mutation • npEiviyqy was found in 8/10 of the B35+ individuals, and two of the B35- individuals—the D–>E substituted peptide had reduced binding affinity to B35 and may be an escape mutant.				
RT (175–183)	RT (329–337)	HPDIVIYQY	in vitro stimulation	human (B35)	Lalvani1997
	• A peptide-based protocol was optimized for restimulation of CTLp using optimized peptide and IL-7 concentrations – importantly this protocol does not stimulate a primary response, only secondary – peptide-specific CTLp counts could be obtained via staining with peptide-Class I tetramers • This peptide was one of the B35 presented test peptides used in control experiments showing that the assay gave no activity using lymphocytes from 21 healthy B35 seronegative donors				
RT (175–183)	RT (328–336 IIIB)	NPDIVIYQY	HIV-1 infection	human (B35)	Menendez-Arias1998, Shiga1996
	• Binds HLA-B*3501 • CTL activity to this epitope was originally detected in a long-term survivor, however it has since been found in normal progressors – it is cross-reactive with HIV-2 (HPDILIYQY), but D3E and V5I substitutions reduce binding [Menendez-Arias1998]				
RT (175–183)	RT (328–336 IIIB)	NPDIVIYQY	HIV-1 infection	human (B35)	Menendez-Arias1998, Sipsas1997
	• HIV IIIB proteins were used to define the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB • NPDIIIYQY, a variant found in HIV-1 JRCSF, was also recognized • NPEIVIYQY, was also recognized • NPDLVIYQY, was also recognized • [Menendez-Arias1998], in a review, notes that the YXDD motif, highly conserved among polymerases, overlaps this epitope – CTL activity to this epitope was originally detected in a long-term survivor, however it has since been found in normal progressors – it is cross-reactive with HIV-2 (HPDILIYQY), but D3E and V5I substitutions reduce binding				
RT (175–183)	RT	NPDIVIYQY	HIV-1 exposed seronegative	human (B35)	Menendez-Arias1998, Rowland-Jones1998a
	• A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating • The A subtype consensus is HPDIVIYQY				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The D subtype consensus is NPEIVIYQY • [Menendez-Arias1998], in a review, notes that the YXDD motif, highly conserved among polymerases, overlaps this epitope – CTL activity to this epitope was originally detected in a long-term survivor, however it has since been found in normal progressors – it is cross-reactive with HIV-2 (HPDILIYQY), but D3E and V5I substitutions reduce binding				
RT (175–183)	Pol (subtype B)	NPDIVIYQY	HIV-1 exposed seronegative	human (B35)	Rowland-Jones1998b
	• HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes • Clade A version of epitope HPDIVIYQY, Clade D NPEIVIYQY				
RT (175–183)	Pol	HPDIVIYQY		human (B35)	Rowland-Jones1999
	• CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5 • In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, and the B35 allele seems to be protective • HIV-2 version of this epitope is not conserved: NPDVILIQY, but the CTLs are cross-reactive – one of five B35 CTL epitopes that are cross-reactive, see also [Rowland-Jones1995b]				
RT (175–183)		HPDIVIYQY	HIV-1 infection	human (B35)	Wilson2000a
	• Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load was also found • All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39 • ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK • The subject with A*0201 had a moderately strong response to SLYNTVATL • Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705 • No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL			
RT (175–183)	Pol (subtype A)	HPDIVIYQY	HIV-1 infection	human (B35)	Kaul2001c
	• This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative • HPDIVIYQY or NPDIVIYQY was recognized in 1 of the 6 women (ML857), and the response was present in the last available sample prior to seroconversion, 7 months • 20/20 sequences of the infecting strain had three substitutions in this epitope, all 20 were NpQiIiyqy, and this form was not recognized by CTL from ML 857 – this was the only case in the study where a virus carrying an unrecognized form of the epitope broke through • The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire • NPDIVIYQY was recognized by 1/22 HEPS control sex workers, ML887				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (175–183)	RT (175–183 SF2)	NPDIVIYQY	HIV-1 infection	human (B35)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-B35+ individuals that had a CTL response to this epitope broken down by group: 1/2 group 1, 0/2 group 2, and 1/1 group 3			
RT (175–183)	Pol (342–350)	HPDIVIYQY	HIV-1 infection, HIV-1 exposed seronegative	human (B35)	Kaul2001a
	• Variants (H/N)PDIVIYQY are specific for the A/B clades • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure • Among HLA-B35 women, 2/3 HEPS and 1/4 HIV-1 infected women recognized this epitope • The dominant response to this HLA allele was to this epitope in only one of the 2/3 HEPS cases, and was not to this epitope in the one responsive HIV-1 infected women • Subject ML 857 shifted from a A*6802 DTVLEDINL and B35 (H/N)PDIVIYQY response prior to seroconversion to a B35 PPIPVGDIY and B35 VPLRPMTY response post-seroconversion and the loss of the pre-seroconversion response was not due to sequence variation within these epitopes			
RT (175–183)		HPDIVIYQY	HIV-1 infection	human (B35)	Sabbaj2002b
	• Epitope name: Pol-HY9 • Among HIV+ individuals who carried HLA B35, 4/21 (19%) recognized this epitope				
RT (175–183)	Pol	NPDIVIYQY	HIV-1 infection	human (B35)	Sabbaj2002a
	• IFNgamma T-cell responses in breast milk of 5 HIV-1 infected women from the US and 6 from Zambia were tested with using Elispot. 11/11 women responded to Gag, 8/11 responded to Pol, 7/11 women to Nef, and 2/5 women to Env peptide pools. These responses were shown to be primarily due to CD8+ T-cells in one woman, and another woman had cytolytic responses measured by Cr-release. • T-cells in breast milk from a volunteer who was HLA A3, A11, B35, B51 induced IFNgamma after stimulation with a peptide that carries known B35 epitope NPDIVIYQY. • The frequencies of responses in the two compartments differed, and 2/4 women that responded to epitopes in Nef 101-205 and Pol 601-710 showed responses in breast milk but no detectable responses in peripheral blood cells.				
RT (175–183)	Pol	HPDIVIYQY	HIV-1 infection, Vaccine	human, macaque (B35)	Hanke2000, Wee2002
	Vaccine *Vector/Type:* DNA prime with vaccinia MVA boost *Strain:* subtype A *HIV component:* p17, p24, polyepitope • The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000].				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].				
RT (175–184)	RT (175–184 LAI)	NPDIVIYQYM	HIV-1 infection	human (B51)	Samri2000
	• This epitope contains the mutation M184V, a frequent mutation induced by nucleoside reverse transcriptase inhibitors • Patient 246#1 (B51), was found by ELISPOT to recognize the wild type and the mutated peptide after zidovudine treatment • The resistance mutation M184V gave an increased predicted binding score to B51 (http://bimas.dcrt.nih.gov/molbio/hla_bind) compared to the wildtype RT sequence and also an increased ELISPOT reactivity				
RT (175–199)	RT (342–366 LAI)	NPDIVIYQYMDDLYVGSDL-EIGQHR	HIV-1 infection	human (A11)	Menendez-Arias1998, Walker1989
	• One of five epitopes defined for RT-specific CTL clones in this study				
RT (179–187)	RT	VIYQYMDDL	Vaccine	human (A*0201)	Hanke1998a, Hanke1998b
	Vaccine *Vector/Type:* vaccinia *HIV component:* polyepitope • This epitope was shown to be processed and presented to appropriate CTL clones upon infection of human target cells with vaccinia virus Ankara (VVA) carrying 20 HIV-1 epitopes recognized by humans				
RT (179–187)	RT	VIYQYMDDL	HIV-1 infection	human (A*0201)	Tan1999
	• Adoptive transfer of two autologous in vitro-expanded CTL clones against the A*0201 restricted epitopes SLYNTVATL and VIYQYMDDL were infused into a patient – they were well tolerated, but the SLYNTVATL clone was shown by tetramer staining to be rapidly eliminated through apoptosis, and the treatment had no impact upon viral load and CD4 and CD8 cell counts • Tetramer staining failed for the VIYQYMDDL epitope as the tetramer was unstable				
RT (179–187)	Pol (346–354)	VIYQYMDDL	HIV-1 infection	human (A*0201)	Sewell1999
	• Proteasome regulation influences epitope processing and could influence patterns of immunodominance • The proteasome is inhibited by lactacystin treatment, and gamma IFN induces expression of proteasome subunits, LMP2 and LMP7, which combine with the proteasome to create an immunoproteasome • IFN-gamma induction of the immunoproteasome and lactacystin inhibition increases the presentation of the A*0201 VIYQYMDDL epitope, but decreases the presentation of the A*0201 ILKEPVHGV epitope, which is immunodominant within pol proteins, showing the two epitopes are processed by different pathways • ILKEPVHGV seems to be processed by the classical proteasome pathway, while VIYQYMDDL appears to be destroyed by this pathway • This epitope contains the catalytic site (YMDD) of RT, a conserved sequence in HIV-1 which restricts escape mutants				
RT (179–187)	RT (346–354 LAI)	VIYQYMDDL	HIV-1 infection	human (A*0201)	Harrer1996a, Menendez-Arias1998
	• The substitution VIYQYVDDL abrogates CTL response and confers drug resistance • [Menendez-Arias1998], in a review, notes that this epitope includes catalytic residues (Asp-185 and Asp-186) in the active site of RT				
RT (179–187)	RT (346–354 LAI)	VIYQYMDDL	HIV-1 infection	human (A*0201)	Brander2001
	• C. Brander notes this is an A*0201 epitope				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (179–187)	RT (346–354)	VIYQYMDDL	HIV-1 infection	human (A*0201)	Brander1998a, Menendez-Arias1998
	• Of 17 infected HLA A*0201 subjects, 13 had CTL responses against the p17 SLYNTVATL epitope, six recognized ILKEPVHGV and five recognized VIYQYMDDL, and there was no correlation between viral load and recognition of a specific epitope or evidence of immune escape • Only one subject had CTL against all three epitopes • Subjects were part of the San Francisco City Clinic Cohort, the ARIEL project and from the Boston area • In the review [Menendez-Arias1998] the authors note that substitution of three residues in this epitope can confer resistance to RT inhibitors (1, 3, and 6) – substitutions V1E and M6V abolish CTL activity, and M6V confers resistance to 3TC – substitution Y3C reduces CTL activity and is associated with resistance to non-nucleoside RT inhibitors				
RT (179–187)	RT	VIYQYMDDL	HIV-1 infection	human (A*0201)	Altfeld2001c
	• Epitope name: RT VL9 • HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested • Three additional previously described HLA-A2 epitopes were added to the set of 20, including RT VL9, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acute infected individuals recognized at least 1 (median of 1 and maximum of 2) • RT VL9 was not recognized by any of the 22 HLA-A2 patients with chronic HIV-1 infection or the 13 HLA-A2 patients with acute HIV-1 infection included in this study				
RT (179–187)	RT (346–354)	VIYQYMDDL	HIV-1 infection	human (A*0201)	Dela Cruz2000
	• Epitope name: VL9 • Integration of HIV RT CTL epitopes into the N-terminus of the HLA-A2 heavy chain, or tethering the epitopes to the target chain, resulted in epitope-specific lysis by CD8+ CTL • These antigens could also be used to stimulate primary responses in vitro				
RT (179–187)	Pol (346–354)	VIYQYMDDL	HIV-1 infection	human (A*0201)	Sewell2002
	• Epitope processing of three different HLA-A*0201 HIV epitopes was shown to use different pathways, which might influence patterns of immunodominance. .174 cells were used that lack TAP1 and TAP2 genes, as well as the LMP2 and LMP7 genes that encode the beta-subunits of the immunoproteasome. These genes could be added back through transfection to study processing. • ILKEPVHGV was efficiently presented in TAP-1 and -2 transfected cells while VIYQYMDDL and SLYNTVATL were not. VIYQYMDDL was destroyed by the MB1 subunit of the protease, and could be expressed in the presence of the proteasome inhibitor lactacystin, but SLYNTVATL expression was not restored. SLYNTVATL expression was unaltered by lactacystin in a wild type cell line.				
RT (179–187)	Pol	VIYQYMDDL	HIV-1 infection, Vaccine	human, macaque (A*0201)	Hanke2000, Wee2002
	Vaccine *Vector/Type:* DNA prime with vaccinia MVA boost *Strain:* subtype A *HIV component:* p17, p24, polyepitope • The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000].				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].				
RT (179–187)	RT	VIYQYMMDL	HIV-1 exposed seronegative	human (A2)	Rowland-Jones1998a
	• A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating • The A and D consensus sequences are both VIYQYMMDL				
RT (179–187)	Pol (346–354)	VIYQYMDDL	Vaccine	human (A2)	Woodberry1999
	Vaccine *Vector/Type:* DNA prime with vaccinia boost *HIV component:* polyepitope • A polyepitope vaccine was generated in a vaccinia construct that contiguously encoded seven epitopes, all presented by HLA A-2 • HHD mice have a transgene of HLA A2 linked to the transmembrane and cytotoxic domains of H-2D^d – this transgene is the only MHC molecule expressed in the mice • CTL responses to Gag (77-85) SLYNTVATL, Pol (476-484) ILKEPVHGV, gp120 (120-128) KLTPLCVTL, and Nef (190-198) AFHHVAREL were observed in HIV polytope HHD-vaccinated mice, and these responses were enhanced with vaccinia boost • No CTL immune responses were generated against HLA A2-restricted HIV epitopes Nef 157-166 (PLTFGWCYKL), Pol 346-354 (VIYQYMDDL), and Nef 180-189 (VLEWRFDSRL) • Sixteen HLA A2+ patients were tested for their ability to make CTL responses by peptide restimulation in culture with the epitopes selected for inclusion in the polytope – one individual recognized all seven of these epitopes; 7 patients had CTL cultures able to recognize at least one of the epitopes, and 6 of those 7 recognized more than one epitope, but they were not able to test all peptides for all patients; many patients only had three peptides tested • VIYQYMDDL was recognized by 3 of the HLA-A2 patients				
RT (179–187)	RT (179–187)	VIYQYMDDL	HIV-1 infection	human (A2)	Schmitt2000
	• The mutation M184V confers resistance to lamivudine, and is in the middle of the HLA-A2 epitope VIYQYMDDL • 1/28 individuals tested produced HIV-1 RT-specific CTL that recognized the peptide representing the lamivudine escape mutants VIYQYVDDL and VIYQYIDDL, but failed to recognize the wildtype epitope VIYQYMDDL • This suggests immunotherapy stimulating anti-VIYQYVDDL responses maybe helpful for reducing lamivudine escape				
RT (179–187)	RT (179–187)	VIYQYMDDL	HIV-1 infection	human (A2)	Haas1998
	• Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively)				
RT (179–187)	Pol (339–347 93TH253 subtype CRF01)	VIYQYMDDL	HIV-1 infection	human (A2)	Sriwanthana2001
	• Epitope name: P334-342 • This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand • HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed • This epitope was reactive in HIV+ control study subject 144 who carried HLA-A2				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (179–187)	Pol (339–347 93TH253 subtype CRF01)	VIYQYMDDL	HIV-1 infection	human (A2)	Bond2001
• More than half of a cohort of HIV+ female sex workers (FSW) from Northern Thailand were HLA-A11 positive, and this study concentrated on A11 epitopes in this group, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested. • 2/4 tested FSWs recognized the E clade version of this epitope, which is identical to the previously defined B clade version VIYQYMDDL • This epitope was conserved in many subtypes, and exact matches were very uncommon					
RT (179–187)	RT (179–187)	VIYQYMDDL	HIV-1 infection	human (A2)	Day2001
• The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person					
RT (179–187)	Pol (346–354 LAI)	VIYQYMDDL	HIV-1 infection	human (A2)	Kelleher2001a
• Ritonavir (RTV) inhibits chymotryptic activity in the 20S proteasome in vitro, as does Saquinavir (SQV) to a lesser extent; Indinavir (IDV) does not. Thus there is concern protease inhibitors may adversely effect CTL epitope processing, but this paper indicates that processing is not inhibited at therapeutically relevant concentrations of RTV when the proteasome is functioning in an intracellular context. • RTV did not alter the presentation two RT A2 epitopes processed by distinct pathways: ILKEPVHGV, generated by the constitutive proteasome containing the MB1 beta subunit, and VIYQYMDDL which is dependent on IFNgamma induction of LMP7 which replaces MB1 in the immunoproteasome, and is destroyed by MB1 in the constitutive proteasome. • RTV did not inhibit the processing and assembly of HLA-B35 or -A2, which are assembled with a rapid and moderate time course, respectively, or of HLA-A3, -B27 and -B39.					
RT (179–187)	Pol (subtype B)	VIYQYMMDL	HIV-1 exposed seronegative	human (A2, A*0202)	Rowland-Jones1998b
• HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes • This epitope is conserved among A, B and D clade viruses					
RT (179–187)	RT (346–354 LAI)	VIYQYMDDL	Vaccine	murine (A2.1)	Peter2001
Vaccine *Vector/Type:* peptide *Strain:* LAI *Adjuvant:* P30, incomplete Freund's adjuvant (IFA), Montanide (ISA 720), PLG-microparticle • Epitope name: LR26 • The stability of peptide binding to HLA-A2.1 was determined for six HLA-A2.1 peptides included in this vaccine study – ILKEPVHGV (RT), SLYNTVATL (p17), SLLNATDIAV (gp41) and LLWKGEGAV (RT) all bound with high affinity comparable to a influenza epitope reference (GILGFVFTL), while RGPGRAFVTI and VIYQYMDDL bound with a lower affinity (relative binding activity = 0.01). • The four high-affinity peptides formed stable complexes with half-lives ranging between 8 and 32 hours, while the low affinity peptides had half lives of less than an hour. • HLA-A2.1 transgenic mice were immunized with the six HIV-1 peptides and P30, as a universal T-helper epitope, with IFA or Montanide or microspheres as adjuvants. • All peptides except VIYQYMDDL induced a stong CTL response in Cr-release assays - stronger responses were observed when peptides were delivered alone, indicating immunodominance when the combination was used.					

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (179–187)	RT (346–354 LAI)	VIYQYMDDL	Vaccine	murine (A2.1)	Peter2002
	Vaccine *Vector/Type:* peptide *Strain:* LAI *Adjuvant:* P30, incomplete Freund's adjuvant (IFA), IL-12 • Epitope name: LR26 • When HIV-1 peptides were used to vaccinate HLA-A2.1 transgenic A2-Kb mice, strong responses to five peptides were observed when the peptides were given individually, but immunodominance limited the response to some of the peptides when they were given in combination [Peter2001]. IL-12 can counteract immunodominance in BALB/c mice, so it was given with the multiple epitope vaccination, and was instead found to specifically eliminate the HLA-A2.1-epitope CTL responses, but not Kb CTL responses. This was possibly a consequence of transient depletion of T-cells, B cells and macropahges in the spleen.			
RT (180–189)	RT (LAI)	IYQYMDDLYV	HIV-1 infection	human (A*0201)	Menendez-Arias1998, vanderBurg1997
	• Recognized by CTL from a progressor, spans important RT functional domain • A previous study determined that this was an epitope recognized by a long-term survivor				
RT (181–189)	RT (181–189 LAI)	YQYMDDLYV	HIV-1 infection	human (A*0201)	Samri2000
	• This epitope contains the mutation M184V, a frequent mutation induced by nucleoside reverse transcriptase inhibitors • High levels of recognition by ELISPOT were observed for zidovudine induced mutation YQYVDDLYV and for the wildtype peptide YQYMDDLYV in patient 250#0 (HLA-A*0201), but neither were recognized by patient 201#5 (also HLA-A*0201) • Both the wild-type and the mutated peptide were computer predicted to have a high binding affinity for A2 (http//bimas.dcrt.nih.gov/molbio/hla_bind)				
RT (192–201)	RT (192–201)	DLEIGQHRTK	HIV-1 infection	human (A3)	Haas1998
	• Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively) • New clusters of epitopes were defined utilizing different HLA molecules				
RT (192–216)	RT (359–383 HXB2)	DLEIGQHRTKIEELRQHLL-RWGLTT	HIV-1 infection	human (Bw60)	Menendez-Arias1998, Walker1989
	• One of five epitopes defined for RT-specific CTL clones in this study				
RT (192–216)	RT (191–215)	DLEIGQHRTKIEELRQHLL-RWGFTT	HIV-1 infection	human (polyclonal)	Haas1997, Menendez-Arias1998
	• Polyclonal CTL recognition switched from RT 191-215 to RT 514-524 when AZT therapy selected for the resistance mutation, and presumably the escape variant, RT T215Y				
RT (198–212)	RT (SF2)	HRTKIEELRQHLLRW	HIV-1 infection	human	Altfeld2000b
	• This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual • The response to the peptide was CD8 dependent, but the HLA presenting molecule and optimal epitope were not determined				
RT (201–209)	RT (201–209)	KIEELRQHL	HIV-1 infection	human (A2)	Haas1998
	• Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively) • New clusters of epitopes were defined utilizing different HLA molecules				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (201–210)	Pol	KIEELRQHLL		human (B58)	De Groot2001
	• The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes • A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes could stimulate IFNγ production in an ELISPOT assay • KIEELRQHLL was newly identified as a HLA-B58 epitope in this study, it had been previously shown to be presented by HLA-A2 and Bw60 • KIEELRQHLL did not bind detectably to B7			
RT (202–210)	RT (202–210 LAI)	IEELRQHLL		human (B*4001)	Altfeld2000b, Brander2001
	• C. Brander notes this is a B*4001 epitope				
RT (202–210)	RT (SF2)	IEELRQHLL	HIV-1 infection	human (B60)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-B60+ individuals that had a CTL response to this epitope broken down by group: 0/2 group 1, 1/1 group 2, and 0/0 group 3			
RT (202–210)	RT (SF2)	IEELRQHLL	HIV-1 infection	human (B60(B*4001)	Altfeld2000b
	• This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes • B60 is present in 10-20% of the Caucasoid and very common in Asian populations				
RT (202–210)	RT (202–210)	IEELRQHLL	HIV-1 infection	human (B60/B61)	Day2001
	• No immunodominant responses were detected to five B61-restricted epitopes tested • All five B60-restricted epitopes were reactive in another subject, and the B60-restricted responses together contributed over one-third of the total CTL response				
RT (203–212)	RT (LAI)	EELRQHLLRW	HIV-1 infection	human (B44)	Menendez-Arias1998, vanderBurg1997
	• The only epitope recognized by CTL from a long-term survivor in two samples taken six years apart • Recognized by CTL from a progressor, EILKEPVGHGV and TWETWWTEYW were also recognized				
RT (209–220)	RT (209–220)	LLRWGLTTPDKK	HIV-1 infection	human (A2)	Haas1998
	• Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively) • New clusters of epitopes were defined utilizing different HLA molecules				
RT (243–252)	RT (LAI)	PIVLPEKDSW	HIV-1 infection	human (B*5701)	Menendez-Arias1998, vanderBurg1997
	• Recognized by CTL from a progressor and a long-term survivor, KITTESIVIW was also recognized				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (243–252)	RT (LAI)	PIVLPEKDSW	HIV-1 infection	human (B*5701)	Menendez-Arias1998, vanderBurg1997
	• Recognized by CTL from long-term survivor, whose CTL response persisted for more than 10 years – the substitution V3M reduced affinity but was well recognized, on the other hand V3T and D8G did not reduce affinity, but abrogated CTL response				
RT (243–252)	RT (410–419)	PIVLPEKDSW	HIV-1 infection	human (B57)	Oxenius2000
	• Epitope name: PIV • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable • None of the 8 study subjects recognized this epitope but none were HLA B57+				
RT (243–252)	RT	PIVLPEKDSW	HIV-1 infection	human (B57)	Oxenius2002b
	• Epitope name: PIV • Using previously defined epitopes [Oxenius2000, Oxenius2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI). • STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.				
RT (244–252)	RT (399–407)	IVLPEKDSW		human (B*5701)	Brander2001
	• Subtype of B57 not determined • C. Brander notes this is a B*5701 epitope				
RT (244–252)	RT (244–252 LAI)	IVLPEKDSW	HIV-1 infection	human (B*5701, B*5801)	Klein1998
	• This peptide was defined as the optimal epitope • B57 has been associated with long-term non-progression in the Amsterdam cohort. • The most pronounced CTL responses in HLA B*5701 LTS were to RT and Gag • B57 restricted CTL responses are targeted at multiple proteins, but one LTS had a response that was dominated by reactivity to the epitope – two variants were found in this LTS: ITLPEKESW, which bound to B*5701 with similar affinity as the index peptide but was an escape mutant that was not recognized by CTL, and IMLPEKDSW, which bound to B*5701 with reduced affinity but could still be recognized • In an additional HIV+ LTS, only the variant IELPEKDSW was found, and this epitope was recognized by CTL but had less affinity for B*5701 than the index peptide • This epitope was recognized in the context of both HLA-B*5701 and B*5801				
RT (244–252)	Pol (244–252)	IVLPEKDSW	HIV-1 infection	human (B*5801)	Appay2000
	• Combined tetramer and intracellular cytokine staining was used to study the function of circulating CD8+ T cells specific for HIV and CMV • HIV-specific CD8+ T cells expressed lower levels of perforin than CMV-specific CD8+ T cells from the same donor, and this was associated with persistent CD27 expression on HIV-specific cells, suggesting impaired maturation • In most donors, between 50% and 95% of the activated virus-specific CD8+ T cells produced IFN-γ and MIP-1β with a distinct subset that failed to produce TNF-α				
RT (244–252)	RT (399–407)	IVLPEKDSW		human (B57)	vanderBurg1997

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (244–252)	RT (244–252)	IVLPEKDSW	HIV-1 infection	human (B57)	Guillon2002
	• An early-expressed Nef protein was modified to contain Env and Pol epitopes to enable the study the effect of expression kinetics on CTL mediated suppression of replication. The "EpiNef" construct was inserted into a recombinant vaccinia virus which was used to infect a target cell line; the target cells were lysed by CTL clones specific for the Env and Pol epitopes indicating that they were properly processed.				
RT (244–252)	RT (244–252 ACH320.2A.2.1)	IVLPEKDSW	HIV-1 infection	(B57)	vanBaalen2002
	• Tat, Rev and Nef are the first HIV proteins expressed upon acute infection of T-cells (< 6 hours), and RT is not expressed until after 24 hours. The B14-restricted Rev-SAEPVPLQL specific CD8 T-cell clone TCC108, and the B57-restricted RT-IVLPEKDSW specific CD8 T-cell clone TCL1C11 were co-incubated with CD4+ cultures innoculated with HIV-1 at low MOI. Co-incubation with the Rev-specific CTL resulted in two logs less HIV-1 production in ten days of culture. When the RT epitope was cloned into the Nef gene of the infecting strain, another early expressed protein, it proved as effective as the Rev epitope at inhibiting viral production. A mathematical model of CTL-target interactions suggest early proteins are important for vaccine design.				
RT (245–252)	Pol	IVPEKDSW	HIV-1 infection	human (B57)	Kostense2001
	• HLA tetramers to six epitopes were used to study HLA-A2, B8 and B57 CTL in 54 patients – HIV-specific tetramer positive cells were inversely correlated with viral load in patients with high CD4, but in patients with CD4 T-cells below 400 high tetramer frequencies were found despite high viral load • Most patients have high levels of HIV-specific T-cell expansions, but many of these cells aren't functional • In 15 of the patients, the proportion of IFN gamma producing tetramer cells correlated with AIDS-free survival				
RT (259–267)	Pol	KLVGKLNWA	HIV-1 infection	human (A2 supertype)	Propato2001
	• Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus • This epitope can bind four of the five HLA-A2 supertypes alleles (A*0201, A*020 2, A*0203, A*0206 and A*6802) • Tetramer staining with A2, beta2microglobulin, and either SLYNTVATL, KLVGKLNWA, or LTFGWCFKL revealed that tetramers detected more HIV-specific sells in LTNP than in progressors, activated effector cells were the minority population, and ELISPOT correlated better with the effector cell subpopulation than the total tetramer stained population				
RT (260–271)	RT (415–426 IIIB)	LVGKLNWASQIY	HIV-1 infection	human (B*1501)	Brander2001
	• C. Brander notes this is a B*1501 epitope				
RT (260–271)	RT (260–271)	LVGKLNWASQIY	HIV-1 infection	human (B62)	Day2001
	• No immunodominant responses were detected to four B62-restricted epitopes tested				
RT (260–271)	RT (415–426 IIIB)	LVGKLNWASQIY	HIV-1 infection	human (Bw62)	Brander1996b, Menendez-Arias1998
	• P. Johnson, Pers. Comm.				
RT (263–271)	RT (263–271 LAI)	KLNWASQIY		human (A*3002)	Brander2001, Goulder2001a
	• C. Brander notes this is an A*3002 epitope				
RT (263–271)	RT	KLNWASQIY	HIV-1 infection	human (A*3002)	Goulder2001a
	• Epitope name: KY9 (RT-35)				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• HLA-A*3002 is very common in African populations, 50% of Zimbabweans express HLA-A30, 44% in African Zulu, so five new HIV epitopes were characterized that are presented by this HLA molecule • A rapid method was developed combining ELISPOT with intracellular IFN-γ staining of PBMCs to map optimal epitopes, then HLA presenting molecules were defined – this method was completed within 48 to 72 hours of receipt of blood • Two individuals were studied: Subject 199 (HLA A*0201/*3002 B*4402/51 Cw2/5), a Caucasian, and Subject 6007 (HLA A*3002/ B53/*5801 Cw4/7) an African-Caribbean • In both HLA-A*3002 individuals the response to RSLYNTVATLY was dominant • In subject 199 four additional A*3002 epitopes were identified • Three quantitative assays, ELISPOT, precursor frequency and chromium release, confirmed a hierarchy of response: RY11 (p17) > KY9 (gp41) > KY9 (RT-53) > IY9 (gp41)			
RT (263–271)	RT	KLNWASQIY	HIV-1 infection	human (A30)	Altfeld2002
	• Epitope name: A30-KY11(RT) • Peripheral blood (PB) and lymph node (LN) CD8+ T-cell responses were compared in 15 asymptomatic HIV-1 infected patients using all known optimal CTL epitopes (http://hiv-web.lanl.gov/content/hiv-db/REVIEWS/brander2001.html) for each person's class I HLA alleles. • 60 epitope responses were detected in both PB and LN samples of the 15 patients, and an additional 8 responses were detected only in LN. The total magnitude of the response was similar in LN and PB, but the percentage of CD8+ T cells in the LN is lower so the number of HIV-specific cells per million CD8+ T-cells is higher in the LN. • 1 year post-HAART treatment in five patients studied, the magnitude of the CD8 T-cell response was decreased in both LN and PB, but more dramatically in PB, and 13/25 epitope responses in the PB became undetectable, in contrast to 5/26 in the LN. • Treatment interruption following HAART resulted in increased viremia accompanied by the restoration of the detection of 13 epitopes that had become undetectable in the PB, and the addition of 9 novel epitope responses. • Breakdowns of epitope responses were shown for 4 individuals. Patient D displayed the greatest response to B27-KK10 (p24), and also responded to A30-RY11(p17), A32-PW10(RT), A30-KY11(RT), A32-RW10(gp120), and B18-YY9(Nef).			
RT (266–285)	Pol (421–440)	WASQIYPGIKVRQLCKLLRG	HIV-1 infection	human	Novitsky2002
	• HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
RT (268–282)	RT (SF2)	SQIYPGIKVRQLCKL	HIV-1 infection	human	Altfeld2001a
	• HIV+ individual AC-06 was tested for reactive overlapping peptides spanning all HIV-1 proteins in an ELISPOT and was found to react with 12 peptides from 7 proteins, suggesting that the breadth of CTL responses are underestimated if accessory proteins are not included in the study • RT peptides SQIYPGIKVRQLCKL and WKGSPAIFQSSMTKI were recognized				
RT (269–277)	Pol (424–432)	QIYAGIKVK	HIV-1 infection	human (A*1101)	Fukada2002
	• binding affinity, inter-clade comparisons • Counterparts for eight known clade B HLA A*1101 epitopes were generated for clade E (CRF01). Three epitopes, identical among clade A-E, were cross-reactive and recognized by clade E infected individuals. The clade E and B analogs to three more HLA A*1101 epitopes was recognized in a clade specific manner. Two other HLA A*1101 clade B defined epitopes were found not to have stimulated a response in clade E infected individuals. • QIYAGIKVK is commonly found in viruses representing subtypes A, B and E. It was strongly recognized by CTL from 1/5 B clade infected Japanese subjects, and 5/7 E clade infected Thai subjects.			

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• QIYAGIKVK had the highest A*1101 binding affinity, but qiyagikvR and qiyPgikvR (the most common C and D clade variant both bound to A*1101). QIYAGIKVK and qiyagikvR were both cross-presented by a clone from a B clade infection, but qiyPgikvR was not.				
RT (269–277)	(LAI)	QIYPGIKVR		(A3)	Altfeld2000a, Brander2001
RT (269–277)	RT (269–277)	QIYPGIKVR	HIV-1 infection	human (A3)	Day2001
	• The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person • All patients recognized at least 1 A3 epitope, up to 8 A3 epitopes, but none was clearly dominant				
RT (269–277)	RT (424–432)	QIYPGIKVR	HIV-1 infection	human (A3)	Yu2002a
	• Epitope name: A3-QR9 • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 1/14 HLA-A3 positive individuals had detectable A3-restricted responses to this epitope during acute infection, but only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 4/7 individuals began to have detectable responses to this epitope after STI.				
RT (271–279)	(LAI)	YPGIKVRQL	HIV-1 infection	human (B*4201)	Brander2001
	• C. Brander notes this is a B*4201 epitope				
RT (271–279)	RT (438–446 IIIB)	YPGIKVRQL	HIV-1 infection	human (B42)	Menendez-Arias1998, Wilson1996
	• YAGIKVRQL and YPGIKVKQL are naturally occurring variants that are both reactive • YHKIKVRQL is a naturally occurring variant that has not been tested • Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study				
RT (271–279)	Pol (438–446 IIIB)	YPGIKVRQL	HIV-1 infection	human (B42)	Wilson1999a
	• This study describes maternal CTL responses in the context of mother-to-infant transmission • Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants • An additional variant that gave a positive CTL response: YPGIKVKQL, YAGIKVRQL • YHGIKVRQL was an escape mutant				
RT (293–301)	RT (448–456 SF2)	IPLTEEAEL	HIV-1 infection	human (B*3501)	Menendez-Arias1998, Tomiyama1997
	• A CTL clone responsive to this epitope was obtained • Only 1/7 B35-positive individuals had a CTL response to this epitope • An E to K substitution at position 5 abrogates specific lysis, but not binding to B*3501 • An I to V substitution at position 1, P to Q at position 2, and E to K at 5, abrogates specific lysis and binding to B*3501 • An I to V substitution at position 1 did not alter reactivity • Reviewed in [Menendez-Arias1998], this epitope lies in the thumb region of RT				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (293–301)	Pol (448–456 SF2-24)	IPLTEEAEL	HIV-1 infection	human (B*3501 AND B*5101)	Tomiyama2000b
	• Epitope name: HIV-B35-SF2-24 • This epitope is naturally processed and presented by both HLA-B*3501 and HLA-B*5101 and is cross-recognized by a single CTL clone • IPLTEEAEL binds approximately four times more tightly to HLA-B*3501 than HLA-B*5101.				
RT (293–301)	Pol (489–456)	IPLTEEAEL	HIV-1 infection	human (B*3501, B*5301, B*5101, B*0702)	Ueno2002
	• The IPLTEEAEL epitope was known to be presented by both HLA-B*3501 and -B*5101 to a dual specific CTL clone. A single TCR complex bearing Valpha12.1 and Vbeta5.6 was shown recognize the epitope in either HLA-B*3501 and -B*5101. Furthermore, this TCR also recognized the peptide presented by B*5301 and B*0702 in cytolytic CTL assays, demonstrating that this single TCR complex recognizes the same peptide presented by a range of HLA class I molecules.				
RT (293–301)	(SF2)	IPLTEEAEL	HIV-1 infection	human (B35)	Kawana1999
	• HLA B35 is associated with rapid disease progression • The sequences of 9 previously described HIV-1 B35 CTL epitopes were obtained in 10 HLA B35+ and 19 HLA B35- individuals • 3/9 CTL epitopes had substitutions that were more common in B35+ individuals than in B35- individuals but this was one of the six that had no B35 associated pattern of mutation				
RT (293–301)	RT (448–456 SF2)	IPLTEEAEL	HIV-1 infection	human (B35, B51)	Menendez-Arias1998, Shiga1996
	• Binds HLA-B*3501 and B*5101 • Reviewed in [Menendez-Arias1998], this epitope lies in the thumb region of RT				
RT (293–301)	Pol (447–455)	IPLTEEAEL	HIV-1 infection, HIV-1 exposed seronegative	human (B51)	Kaul2001a
	• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers				
RT (294–318)	RT (461–485 HXB2)	PLTEEAELELAENREILKE-PVHGVY	HIV-1 infection	human (A2)	Menendez-Arias1998, Walker1989
	• One of five epitopes defined for RT-specific CTL clones in this study				
RT (308–317)	RT (LAI)	EILKEPVGHV	HIV-1 infection	human (A*0201)	Menendez-Arias1998, vanderBurg1997
	• Recognized by CTL from a long-term survivor, SPIETVPVKL was also recognized • Recognized by CTL from a progressor, EELRQHLLRW and TWETWWTEYW were also recognized				
RT (309–317)	RT (476–484 LAI)	ILKEPVHGV	HIV-1 infection	human	Luzuriaga2000
	• Longitudinal study of 8 infants with prolonged viral suppression due to combination antiretroviral therapy showed no HIV-1 specific CTL responses in peripheral blood cells. 6/8 were studied using a Chromium release assay and no response was detected using Gag expressed in vaccinia in the target cells. Three HLA-A*0201 children were tested using SLYNTVATL or ILKEPVHGV HLA A*0201 tetramers and again no HIV-specific response was detected, either using PBMC specimens, or PBMC which had been stimulated in vitro for a week.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• In contrast, one of the children with suppressed HIV viral replication who was co-infected with HIV and EBV, while HIV-tetramer negative, had EBV-tetramer staining cells at a frequency of 0.14% in the PBMC.				
RT (309–317)	RT (476–484)	ILKEPVHGV	HIV-1 infection	human (A*02)	Huang2000
	• The single cell ELISPOT assay was optimized and highly specific, and found to work well even after the primary cells had been frozen and thawed • Increases in gamma interferon producing cells were observed in response to anti-retroviral therapy using single cell IFN-gamma-production ELISPOT				
RT (309–317)	RT (476–484)	ILKEPVHGV	HIV-1 infection	human (A*02)	Rinaldo2000
	• Administration of triple-drug antiretroviral therapy (IDV, 3TC and ZDV) sometimes showed a transient increase and other times failed to increase CTL responses in patients with advanced HIV disease, but there is a stable population of tetramer stained HIV-specific CD8+ CD45RO+ cells that persist after therapy and long periods of virus being below the level of detection				
RT (309–317)	RT	ILKEPVHGV	HIV-1 infection	human (A*02)	Scott-Algara2001
	• Epitope name: IV9 • This study examined with CTL response in HLA A*02+ children by tetramer staining for HLA-A2 immunodominant epitopes SLYNTVATL and ILKEPVHGV • 71% of the 28 HIV-1 infected HLA-A*02 positive children recognized both epitopes, with cells from 26 children stained positive by the gag tetramer (SLYNTVATL) and 21 children by the pol tetramer (ILKEPVHGV) • There were no differences observed in children that had therapy versus those that did not • Tetramer-binding cells were memory activated CD28-, CD45RO+, CD45RA- HLADR+, CD69-, CD8+ T-cells				
RT (309–317)		ILKEPVHGV	HIV-1 infection	human (A*0201)	Wilson2000a
	• Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load was also found • All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39 • ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK • The subject with A*0201 had a moderatly strong response to SLYNTVATL • Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705 • No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL				
RT (309–317)	Pol (476–484)	ILKEPVHGV	HIV-1 infection	human (A*0201)	Spiegel2000
	• High levels of CD8+ HIV-1 specific and cytomegalovirus specific CTL were detected by HLA-A*0201-peptide tetramers in 3 infected subjects with very low CD4 counts, but CD8 T cell mediated effector activity was not seen • Thus HIV-1 specific CD8+ cells may be present but may lack direct effector activity in late disease, suggesting that overcoming antigen unresponsiveness may be a useful therapeutic strategy				
RT (309–317)	Pol (476–484)	ILKEPVHGV	HIV-1 infection	human (A*0201)	Sewell1999
	• Proteasome regulation influences epitope processing and could influence immunodominance • The proteasome is inhibited by lactacystin treatment, and gamma IFN induces expression of proteasome subunits, LMP2 and LMP7, which combine with the proteasome to create an immunoproteasome				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• IFN-gamma induction of the immunoproteasome and lactacystin inhibition increases the presentation of the A*0201 VIYQYMDDL epitope, but decreases the presentation of the A*0201 ILKEPVHGV epitope, which is immunodominant within pol proteins, showing the two epitopes are processed by different pathways • ILKEPVHGV seems to be processed by the classical proteasome pathway, while VIYQYMDDL appears to be destroyed by this pathway • This epitope contains the catalytic site (YMDD) of RT, a conserved sequence in HIV-1 which restricts escape mutants				
RT (309–317)	Pol (476–484)	ILKEPVHGV	HIV-1 infection	human (A*0201)	Loing2000
	• The ILKEPVHGV was modified by the addition of an N-palmitoyl-lysine residue at the P0, P1 or P10 positions of the parent peptide to create a lipopeptide for direct antigen delivery to the cytoplasm for processing • The N-terminal modification increased the life span for functional CTL recognition up to 48 hours in comparison to the parent peptide				
RT (309–317)	Pol (510–518)	ILKEPVHGV	Vaccine	human (A*0201)	Larsson1999
	Vaccine *Vector/Type:* vaccinia, canarypox *HIV component:* Gag, Pol, Nef, Env • ELISPOT was used to assay the CD8 T cell response to the HIV-1 proteins Gag, Pol, Nef or Env expressed in vaccinia or canarypox vectors in 19 HIV+ people • The highest CTL frequency was directed at epitopes in Pol • In A*0201 individuals, higher numbers of spot-forming T cells were directed against HIV-1 proteins expressed in vaccinia than to peptides SLYNTVATL and ILKEPVHGV presented by A2				
RT (309–317)	RT (476–484)	ILKEPVHGV	HIV-1 infection	human (A*0201)	Wilson1998a
	• HIV+ individuals were followed longitudinally using MHC tetramers in combination with 14 anti-BV chain MAbs, and clonal expansion of HIV-specific T cells was followed in vivo • Seven HIV+ people were studied, and all showed expansions of particular TCR BV clones, often several, relative to uninfected controls • Three patients were followed in detail, TCR VB expansions persisted for 2 to 3 years, with occasional transient increases				
RT (309–317)	RT (476–484)	ILKEPVHGV	HIV-1 infection	human (A*0201)	Betts2000
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes • 2/11 of the A2+ individuals responded to ILKEPVHGV, and neither of these two responded to SLYNTVATL				
RT (309–317)	Pol	ILKEPVHGV	HIV-1 infection	human (A*0201)	Gray1999
	• Administration of highly active antiretroviral therapy (HAART) reduced CD8+ cell frequency, and the CD8+ cells detected by tetramer staining were likely to be memory cells, indicating that persistently replicating viral populations are needed to maintain high frequencies of HIV-1 specific CTL				
RT (309–317)	RT (476–484)	ILKEPVHGV	HIV-1 infection	human (A*0201)	Menendez-Arias1998, Ogg1998b
	• HLA-tetrameric complexes were used in a cross-sectional study of 14 untreated HLA A*0201 positive individuals, revealing an inverse relationship between HIV Gag and Pol specific CTL effector cells (CTLe) and viral load • Inclusion of both the p17 SLYNTVATL and RT ILKEPVHGV epitopes gives a good representation of HLA A*0201-restricted activity • No correlation was observed between the CTLe and CD4 count or clearance rate of productively infected cells				
RT (309–317)	RT	ILKEPVHGV	Vaccine	human (A*0201)	Hanke1998a, Hanke1998b
	Vaccine *Vector/Type:* vaccinia *HIV component:* polyepitope • This epitope was shown to be processed and presented to appropriate CTL clones upon infection of human target cells with vaccinia virus Ankara (VVA) carrying 20 HIV-1 epitopes recognized by humans				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (309–317)	RT (476–484)	ILKEPVHGV	in vitro stimulation	human (A*0201)	Konya1997, Menendez-Arias1998
	• This epitope was included as a positive control • Binding affinity to A*0201 was measured, $C\_1/2\max\mu M = 12$				
RT (309–317)	RT (468–476)	ILKEPVHGV	in vitro stimulation	human (A*0201)	vanderBurg1996
	• Immunogenic in humans, slow dissociation rate, and associated with immunogenicity in transgenic HLA-A*0201/K^b mice • CTL generated by in vitro stimulation of PBMC derived from uninfected individual				
RT (309–317)	RT (468–476)	ILKEPVHGV	in vitro stimulation	human (A*0201)	vanderBurg1995
	• Binds HLA-A*0201 – CTL generated by in vitro stimulation of PBMC from an HIV negative donor				
RT (309–317)	RT (476–484)	ILKEPVHGV	HIV-1 infection	human (A*0201)	Menendez-Arias1998, Pogue1995
	• Mutational study: position 1 I to Y increases complex stability with HLA-A*0201				
RT (309–317)	RT (476–484)	ILKEPVHGV	HIV-1 infection	human (A*0201)	Goulder1997e, Goulder1997a, Menendez-Arias1998
	• Identical twin hemophiliac brothers were both infected with the same batch of factor VIII • One had a response to gag A2 epitope SLYNTVATL, the other to pol A2 epitope ILKEPVHGV • Viral sequencing from the twin that had no response to SLYNTVATL indicated his virus had the substituted form SLHNAVAVL • 71% of an additional set of 22 HIV-1 infected HLA-A*0201 positive donors preferentially responded to gag SLYNTVATL • Those individuals with a pol ILKEPVHGV response tended to have mutations in or around SLYNTVATL • [Goulder1997a] is a review of immune escape that summarizes this study				
RT (309–317)	RT (309–317)	ILKEPVHGV	HIV-1 infection	human (A*0201)	Altman1996
	• This paper introduces the tetramer methodology which permits quantification of specific CTL based on expression of specific TCRs—HLA-A2 tetramers were prepared that can stain CTL lines specific for ILKEPVHGV and SLYNTVATL, and can quantify HIV-specific CD8+ cell lines in freshly isolated PBMCs. • Three patients only stained the Gag epitope SLYNTVATL, one patient had the highest frequency of tetramer staining to the Pol epitope (0.77%), less to the Gag epitope (0.28%) • The A2-Pol CD8+ clones were CD45RO positive and HLA-DR and CD38 negative, suggesting a memory rather than effector phenotype				
RT (309–317)	RT (476–484)	ILKEPVHGV	in vitro stimulation	human (A*0201)	Menendez-Arias1998, Walter1997
	• HLA-A2 heavy chain and β2-microglobulin expressed in E. coli were refolded in the presence of this peptide • The HLA-A2-peptide complex elicited HLA-A2 peptide-specific CTL response in cells lacking HLA-A2 • Suggests that preformed HLA-peptide complexes could provide an alternate to intracellular processing for immunogens				
RT (309–317)	RT (464–472)	ILKEPVHGV	HIV-1 infection	human (A*0201)	Gray1999
	• Peptide-tetramer complexes of A*0201 and SLYNTVATL or ILKEPVHGV were used to study individuals receiving HAART to determine the frequency of Class I HLA-restricted anti-HIV CD8+ T cells • 17/18 asymptomatic patients had a CTL response to one or both epitopes – 72% had a CTL response to SLYNTVATL • After HAART, the majority of the epitope-specific CTL were apparently memory cells				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (309–317)	RT (476–484)	ILKEPVHGV	HIV-1 infection	human (A*0201)	Brander1998a, Brander2001
	• Of 17 infected HLA A*0201 subjects, 13 had CTL responses against the p17 SLYNTVATL epitope, six recognized ILKEPVHGV and five recognized VIYQYMDDL, and there was no correlation between viral load and recognition of a specific epitope or evidence of immune escape • Only one subject had CTL against all three epitopes • Subjects were part of the San Francisco City Clinic Cohort, the ARIEL project and from the Boston area • C. Brander notes this is an A*0201 epitope				
RT (309–317)	Pol (476–484)	ILKEPVHGV	HIV-1 infection	human (A*0201)	Ogg1999
	• CTL effector levels were measured after potent ARV therapy using HLA-tetramer complexes for the A*0201 epitopes SYLVTVATL and ILKEPVHGV in seven patients, and the B*3501 epitope DPNPQEVVL in one additional patient • Levels of CTL effectors typically decline for 5-7 days and then rebound, fluctuating during the first two weeks of therapy • After the early fluctuation, there was a steady exponential decay with a median half-life of 45 days				
RT (309–317)	RT (476–484 LAI)	ILKEPVHGV	HIV-1 infection	human (A*0201)	Brander2001
	• C. Brander notes this is a A*0201 epitope				
RT (309–317)	RT (476–484)	ILKEPVHGV	HIV-1 infection, in vitro stimulation	human (A*0201)	Dela Cruz2000
	• Epitope name: IV9 • Integration of HIV RT CTL epitopes into the N-terminus of the HLA-A2 heavy chain, or tethering the epitopes to the target chain, resulted in epitope-specific lysis by CD8+ CTL • These antigens could also be used to stimulate primary responses in vitro				
RT (309–317)	RT (309–317)	ILKEPVHGV	HIV-1 infection	human (A*0201)	Samri2000
	• Epitope name: P1 • The epitope was recognized by patient 250#0 but not in another A*0201+ patient, 201#5, in a study of the effects of therapy escape mutations on CTL recognition				
RT (309–317)	Pol (LAI)	ILKEPVHGV	in vitro stimulation	human (A*0201)	Engelmayer2001
	• Recombinant canarypox virus vector containing HIV-1 sequences, upon infection of mature dendritic cells, can trigger specific lysis through in vitro by T-cells from HIV-1 infected individuals at levels comparable to the response seen to HIV carried in vaccinia vectors • Recombinant canarypox virus vector containing HIV-1 sequences can also stimulate HIV-specific CD4+ helper T-cell responses				
RT (309–317)	Pol	ILKEPVHGV	HIV-1 infection	human (A*0201)	Gea-Banacloche2000
	• In a study including many long-term non-progressors, no correlation between plasma virus levels and number of HIV-specific CD8+ T-cells was found • High frequencies of circulating CD8+ T-cells were HIV-1 specific, and the majority of these responses were to gag-pol gene products • 4/21 subjects were HLA-(A*0201), and of these only 2 subjects (patient 3 and 19) tested positive to this epitope				
RT (309–317)	Pol (476–484)	ILKEPVHGV	HIV-1 infection	human (A*0201)	Jin2000a
	• The CTL effector levels (CTLe) were compared in long term non-progressors (LTNP) with low viral load and in patients whose virus was well-suppressed by therapy, using a tetramer assay • LTNPs have high memory CTLe numbers and low viral load, while HAART patients had low CTLe numbers and low viral load				
RT (309–317)	Pol (476–484)	ILKEPVHGV	HIV-1 infection	human (A*0201)	Appay2000
	• Combined tetramer and intracellular cytokine staining was used to study the function of circulating CD8+ T cells specific for HIV and CMV				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• HIV-specific CD8+ T cells expressed lower levels of perforin than CMV-specific CD8+ T cells from the same donor, and this was associated with persistent CD27 expression on HIV-specific cells, suggesting impaired maturation • In most donors, between 50% and 95% of the activated virus-specific CD8+ T cells produced IFN-γ and MIP-1β with a distinct subset that failed to produce TNF-α				
RT (309–317)	Pol	ILKEPVHGV	HIV-1 infection	human (A*0201)	Ostrowski2000
	• The role of CD4+ T-cell help in expansion of virus-specific memory CTL was studied through co-culture *ex vivo* • Optimal expansion of HIV-1-specific memory CTL depended on CD4+ T cell help in 9 of 10 patients – CD40 ligand trimer (CD40LT) could enhance CTL in the absence of CD4+ T cell help to a variable degree in most of patients • Those CTL that didn't respond to CD40LT could expand with IL2 present, and IL15 produced by dendritic cells also contributes • The T-helper epitope used for CD4+ T cell stimulation was the universal tetanus helper epitope TET830-843 (QYIKANSKFIGITE)				
RT (309–317)	RT (309–317)	ILKEPVHGV	Vaccine	human, murine (transgenic) (A*0201)	Guardiola2001
	Vaccine *Vector/Type:* HIV-1 peptide in filamentous bacteriophage major coat protein *HIV component:* RT peptide • Epitope name: RT2 • HLA-A2 transgenic mice were injected with bacteriophage antigens expressing a Th epitope and the HIV CTL epitope ILKEPVHGV, and epitope-specific cytotoxic activity was induced.				
RT (309–317)	Pol (476–484)	ILKEPVHGV	HIV-1 infection	human (A*0201)	Sewell2002
	• Epitope processing of three different HLA-A*0201 HIV epitopes was shown to use different pathways, which might influence patterns of immunodominance. .174 cells were used that lack TAP1 and TAP2 genes, as well as the LMP2 and LMP7 genes that encode the beta-subunits of the immunoproteasome. These genes could be added back through transfection to study processing. • ILKEPVHGV was efficiently presented in TAP-1 and -2 transfected cells while VIYQYMDDL and SLYNTVATL were not. VIYQYMDDL was destroyed by the MB1 subunit of the protease, and could be expressed in the presence of the proteasome inhibitor lactacystin, but SLYNTVATL expression was not restored. SLYNTVATL expression was unaltered by lactacystin in a wild type cell line.				
RT (309–317)	Pol	ILKEPVHGV	HIV-1 infected monocyte-derived	murine (A*0201)	Poluektova2002
	• Epitope name: IL-9 • Nonobese diabetic NOD-C.B-17 SCID mice were reconstituted with HLA-A*0201 positive human PBL and injected with HIV-1 infected monocyte-derived macrophages MDM in the basal ganglia to provide a mouse model of HIV-1 encephalitis. • HLA-A*0201 CTL responses were detected by tetramer staining in the spleen in seven days, increased through day 14, and the numbers of productively infected were reduced >85% in the second week.				
RT (309–317)	RT (309–317)	ILKEPVHGV	Vaccine	murine (transgenic) (A*0201)	Boissonnas2002
	Vaccine *Vector/Type:* peptide *HIV component:* RT *Adjuvant:* CFA • Ten naturally occurring variants of the Nef epitope VLMWQFDSRL were tested for their affinity to HLA-A*0201 and for their ability to induce gamma-IFN and cytotoxic functions through vaccination of HLA-A*0201 transgenic mice. • ILKEPVHGV could induce HLA-A*0201 vaccine responses, and was a positive control.				
RT (309–317)	Pol (468–476)	ILKEPVHGV	Vaccine	murine (A*0201)	Singh2002, Sykes1999
	Vaccine *Vector/Type:* DNA *HIV component:* HIV-1 divided into a 32 plasmids in a ubiquitin expression library				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• C3H (H-2k) transgenic mice carrying a fused HLA-A*0201 alpha1 and alpha2 and H-2Dk alpha3 hybrid class I molecule were immunized using an epidermal gene gun with an ubiquitin expression library of 32 plasmids that spanned the HIV-1 genome. Ubiquitin targets the expressed HIV-1 peptides to the proteasome. • A single immunization with the UB-HIV-1 library vaccine induced potent, stable and multivalent CTL responses against all library members. • Immunodominant epitopes SLYNTVATL (Gag), ILKEPVHGV(Pol), RIQRGPGRAFVTIGK(P18) and AFHHVAREK (Nef) elicited strong CD8+/IFN- responses and stimulated CTL that were functional in a Cr-release assay and against wild type antigen. • The presence of multiple plasmids HLA-A*0201-restricted CTL epitopes did not decrease CTL immunogenicity, and CTL responses to single peptide immunizations were comparable to responses based on mixtures of either 16 or 32 peptides.				
RT (309–317)	Pol	ILKEPVHGV	HIV-1 infection, Vaccine	human, macaque (A*0201)	Hanke2000, Wee2002
	Vaccine *Vector/Type:* DNA prime with vaccinia MVA boost *Strain:* subtype A *HIV component:* p17, p24, polyepitope • The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000]. • Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].				
RT (309–317)	RT (476–484 LAI)	ILKEPVHGV	HIV-1 infection	human (A*0201, A*0205)	Mollet2000
	• Epitope name: P1 • A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using tetramer staining or CD8+ cell IFNgamma production to measure responses • In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished • Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change				
RT (309–317)		ILKEPVHGV	HIV-1 infection	human (A02)	Sabbaj2002b
	• Epitope name: Pol-IV9 • Among HIV+ individuals who carried HLA A02, 9/29 (31%) recognized this epitope				
RT (309–317)	Pol (476–484)	ILKEPVHGV	Vaccine	human (A2)	Woodberry1999
	Vaccine *Vector/Type:* vaccinia *HIV component:* polyepitope • A polyepitope vaccine was generated in a vaccinia construct that contiguously encoded seven epitopes, all presented by HLA A-2 • HHD mice have a transgene of HLA A2 linked to the transmembrane and cytotoxic domains of H-2D^d – this transgene is the only MHC molecule expressed in the mice • CTL responses to Gag (77-85) SLYNTVATL, Pol (476-484) ILKEPVHGV, gp120 (120-128) KLTPLCVTL, and Nef (190-198) AFHHVAREL were observed in HIV polytope HHD-vaccinated mice, and these responses were enhanced with vaccinia boost				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• No CTL immune responses were generated against HLA A2-restricted HIV epitopes Nef 157-166 (PLTFGWCYKL), Pol 346-354 (VIYQYMDDL), and Nef 180-189 (VLEWRFDSRL) • Sixteen HLA A2+ patients were tested for their ability to make CTL responses by peptide restimulation in culture with the epitopes selected for inclusion in the polytope – one individual recognized all seven of these epitopes; 7 patients had CTL cultures able to recognize at least one of the epitopes, and 6 of those 7 recognized more than one epitope, but they were not able to test all peptides for all patients; many patients only had three peptides tested • ILKEPVHGV was recognized by 2 of the patients				
RT (309–317)	RT (476–484)	ILKEPVHGV	HIV-1 infection	human (A2)	Kolowos1999
	• TCR usage in CTL specific for this epitope was examined in three patients and identical Vbeta6.1 and Valpha2.5 gene segments were used and two of the patients had very similar complementarity-determining regions – clonal expansion of RT-HIV-specific CTL can contribute to the skewed TCR repertoire in HIV-1 infected patients • CTL clones from all three patients showed similar sensitivity to mutation in the epitope, ilkepvhEv was well recognized (the sequence from SF2), ilkDpvhgv was not (the common A clade form)				
RT (309–317)	RT (476–484)	ILKEPVHGV	HIV-1 infection	human (A2)	Collins1998
	• Nef down-regulates MHC class I molecules, which inhibits CTL killing of HIV-infected targets • The anti-RT CTL clone killed Nef- cells less efficiently than anti-gag clones, correlated with the reduced expression of RT				
RT (309–317)	RT (476–484 LAI)	ILKEPVHGV	HIV-1 infection	human (A2)	Fan1997
	• The capacity of dendritic cells to process and present antigen and stimulate anti-HIV-1 CTL memory responses was studied				
RT (309–317)	RT (464–472)	ILKEPVHGV	HIV-1 infection	human (A2)	Kundu1998b
	• Allogeneic dendritic cells (DCs) were obtained from HLA-identical siblings, pulsed with rgp160 MN or A2-restricted HIV-1 epitope peptides, and infused monthly into six HIV-infected patients • 1/6 showed increased env-specific CTL and increased lymphoproliferative responses, 2/6 showed increase only in proliferative responses, and 3/6 showed no change – pulsed DCs were well tolerated • ILKEPVHGV is a conserved HLA-A2 epitope included in this study – 5/6 patients had this sequence as their HIV direct sequence, and these had a detectable CTL response– one person carried the form ILREPVHGV and had no detectable CTL				
RT (309–317)	RT (476–484)	ILKEPVHGV	HIV-1 infection	human (A2)	Menendez-Arias1998, Tsomides1994
	• CTL clones recognize naturally processed peptide – peptide abundance corresponded to level of CTL killing				
RT (309–317)	RT (476–484)	ILKEPVHGV	HIV-1 exposed seronegative	human (A2)	Rowland-Jones1998a
	• A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating • The A subtype consensus is ILKDPVHGV • The D subtype consensus is identical to the epitope ILKEPVHGV				
RT (309–317)	RT (476–484)	ILKEPVHGV	HIV-1 infection	human (A2)	Cao1997a, Menendez-Arias1998
	• The consensus peptides of B and D clade viruses and some As have the sequence ILKEPVHGV • The consensus peptide of a subset of A clade viruses, ILKDPVHGV, is not cross-reactive				
RT (309–317)	RT (476–484)	ILKEPVHGV	HIV-1 infection	human (A2)	Menendez-Arias1998, Yang1996
	• CD4+ cell lines acutely infected with HIV were studied to determine their susceptibility to lysis by CTL • Clones specific for RT lysed HIV-1 infected cells at lower levels than Env or Gag specific clones				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The distinction was thought to be due to lower expression of RT relative to Env and Gag • CTL can lyse infected cells early after infection, possibly prior to viral production				
RT (309–317)	RT (476–484)	ILKEPVHGV	HIV-1 infection	human (A2)	Yang1997a
	• CTL inhibit HIV-1 replication at effector cell concentrations comparable to those found in vivo • CTL produced HIV-1-suppressive soluble factors – MIP-1α, MIP-1β, RANTES, after antigen-specific activation • CTL suppress HIV replication more efficiently in HLA-matched cells				
RT (309–317)	RT (309–317)	ILKEPVHGV	HIV-1 infection	human (A2)	Menendez-Arias1998, Moss1995
	• Two clones were obtained with different TCR usage, V_β1 and V_β21				
RT (309–317)	RT (476–484)	ILKEPVHGV	HIV-1 infection	human (A2)	Menendez-Arias1998, Musey1997
	• Cervical CTL clones from an HIV-infected woman recognized this epitope				
RT (309–317)	RT (476–484 LAI)	ILKEPVHGV	HIV-1 infection	human (A2)	Menendez-Arias1998, Tsomides1991
	• Precise identification of the nonamer that binds to A2				
RT (309–317)	RT (476–484 LAI)	ILKEPVHGV	Peptide-HLA interaction	human (A2)	Connan1994, Menendez-Arias1998
	• Promotes assembly of HLA-A2 molecules in T2 cell lysates				
RT (309–317)	RT (510–518)	ILKEPVHGV	in vitro stimulation	human (A2)	Parker1992
	• Studied in the context of HLA-A2 peptide binding				
RT (309–317)	Pol (476–484)	ILKEPVHGV	HIV-1 infection	human (A2)	Dyer1999
	• CTL specific responses were measured over a 1.3 to 1.5 year period in members of the Sydney Blood Bank Cohort (SBBC) who had been infected with a natural attenuated strain of HIV-1 which was Nef-defective • Some of these patients had prolonged high levels of CTL effector and memory cells despite low viral load				
RT (309–317)	RT (476–484)	ILKEPVHGV	in vitro stimulation	human (A2)	Zarling1999
	• This study compares the ability of macrophages and dendritic cells to stimulate primary responses in CD8+ lymphocytes isolated from HLA-appropriate HIV-uninfected donors using peptide-pulsed APC – the dendritic cells performed better as APC for the stimulation of primary responses • Strong CTL responses were elicited by the epitopes DRFYKTLRA and GEIYKRWII when presented by either immature or mature dendritic cells – macrophages were not able to prime a CTL response against DRFYKTLRA • A weak response to KLTPLCVSL was stimulated using macrophages as the APC • No detectable response was observed for the following previously-defined HIV epitopes: KIRLRPGGK, ILKEPVHGV, IRLRPGGK, GPKVKQWPL				
RT (309–317)	RT (480–)	ILKEPVHGV	computer prediction	(A2)	Schafer1998
	• This study uses EpiMatrix for T cell epitope prediction to identify possible HLA-B27 and A-2 CTL epitopes in HIV • Based on EpiMatrix predictions, 28 peptides were synthesized and tested using T2 binding assays for potential HLA A2 or B27 binding, and 12 of these were shown to bind to the predicted HLA molecule • Two of these 12 peptides had been previously identified as CTL epitopes: HLA-B27 KRWILGLNK and HLA-A2 ILKEPVHGV • This sequence is not conserved between clades, but is found only in a small number of B clade isolates				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (309–317)	RT	ILKEPVHGV	HIV-1 infection	human (A2)	Altfeld2001c
	• Epitope name: RT IV9 • HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested • Three additional previously described HLA-A2 epitopes were added to the set of 20, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acute infected individuals recognized at least 1 (median of 1 and maximum of 2) • This peptide binds to four HLA-A2 supertype alleles: A*0201, A*0202, A*0206 (highest affinity) and A*6802 • RT IV9 was recognized in 7/22 patients with chronic HIV-1 infection • 1/13 patients with acute HIV-1 infection recognized RT IV9			
RT (309–317)	Pol (subtype A)	ILKDPVHGV	HIV-1 infection	human (A2)	Kaul2001c
	• This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative • ILKDPVHGV or ILKEPVHGV was recognized in 1 of the 6 women (ML1760), and the response was present in the last available sample prior to seroconversion, 12 months • 20/20 sequences of the infecting strain had no substitutions in this epitope, all were ILKDPVHGV, so there was no evidence for escape • The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire • This epitope was recognized by 4/22 HEPS control sex workers: ML887, ML1192, ML1250, and ML1749			
RT (309–317)	RT (476–484)	ILKEPVHGV	HIV-1 infection	human (A2)	Oxenius2000
	• Epitope name: ILK • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable • One of the 2/8 HLA-A2+ study subjects recognized this CTL epitope • Patient SC9 (HLA A1/2, B8/13, Cw0/0701, DR2/11, DQ6/7) had a CTL response against epitopes FLKEKGGL, ILKEPVHGV, SQRRQDILDLWIYHTQGYFPDWQNY, and GEIYKRWII peptides and all responses declined during therapy initiated at day 390 but were restored when therapy become intermittent			
RT (309–317)	Pol	ILKEPVHGV	HIV-1 infection	human (A2)	Kostense2001
	• HLA tetramers to six epitopes were used to study HLA-A2, B8 and B57 CTL in 54 patients – HIV-specific tetramer positive cells were inversely correlated with viral load in patients with high CD4, but in patients with CD4 T-cells below 400 high tetramer frequencies were found despite high viral load • Most patients have high levels of HIV-specific T-cell expansions, but many of these cells aren't functional • In 15 of the patients, the proportion of IFN gamma producing tetramer cells correlated with AIDS-free survival			
RT (309–317)	Pol	ILKEPVHGV	HIV-1 infection	human (A2)	Seth2001
	• CTL responses were studied by tetramer staining in 41 patients with combination therapy – activated CD8+ T-cells decline as the viral load drops in response to therapy, but the overall level of antigen-specific cells capable of differentiating into effectors stays constant and new epitopes may be recognized • 6/10 A*0201+ individuals had HIV-specific tetramer staining cells, and 5 of these declined upon successful therapy • 3/10 A*0201+ individuals with chronic HIV-1 infection recognized this epitope			

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Prior to therapy, the mean percentage of CD8+ cells that recognized the immunodominant epitope SLYNVATL was six-fold greater than the percentage recognizing the epitope ILKEPVHGV				
RT (309–317)	RT (476–484 SF2)	ILKEPVHGV	HIV-1 infection	human (A2)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-A2+ individuals that had a CTL response to this epitope broken down by group: 1/10 group 1, 0/6 group 2, and 3/4 group 3				
RT (309–317)	Pol (476–484)	ILKDPVHGV	HIV-1 infection, HIV-1 exposed seronegative	human (A2)	Kaul2001a
	• Variants ILK(D/E)PVHGV are A/B clade specific • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure • Among HLA-A2 women, 7/10 HEPS and 14/26 HIV-1 infected women recognized this epitope, and ILK(D/E)PVHGV tended to be more reactive in HEPS women, SL(F/Y)NTVATL in infected women • The dominant response to this HLA allele was to this epitope in all 7/10 HEPS cases but in only 5 of the 14/26 HIV-1 infected women • Four epitopes were considered to be "resistant epitopes", as they were preferentially reactive in HEPS women and so may confer resistance, and these were found in three different proteins: A2 ILK(D/E)PVHGV in RT, A*6802 DTVLEDINL in Protease, B14 DLN(M/T)LN(I/V)V in p24 and B18 FRDYVDRF(Y/F)K also in p24 • Differences in epitope specificity were only seen for responses restricted by class I HLA alleles A2, A24, A*6802, B14, and B18, previously shown to be associated with resistance to HIV-1 in this cohort • Subject ML 1250 had an A2 response to ILK(D/E)PVHGV prior to seroconversion, which switched to SL(F/Y)NTVATL post-seroconversion • Subject ML 1760 had an A2 response to ILK(D/E)PVHGV prior to seroconversion, and gained responses to epitopes A2 SL(F/Y)NTVATL and B27 KRWII(L/M)GLNK post-seroconversion				
RT (309–317)	Pol (93TH253 subtype CRF01)	ILRIPVHGV	HIV-1 infection	human (A2)	Sriwanthana2001
	• Epitope name: P464-472 • This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand • HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed • This epitope was reactive in HIV+ control study subject 144 who carried HLA-A2				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (309–317)	Pol (93TH253 subtype CRF01)	ILRIPVHGV	HIV-1 infection	human (A2)	Bond2001
	• More than half of a cohort of HIV+ female sex workers (FSW) from Northern Thailand were HLA-A11 positive, and this study concentrated on A11 epitopes in this group, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested. • 1/4 tested FSWs recognized the E clade version of this epitope, which differs from the previously defined B clade version by two amino acids: ILKEPVHGV • This epitope was not conserved in many subtypes, and exact matches were very rare				
RT (309–317)	RT (309–317)	ILKEPVHGV	HIV-1 infection	human (A2)	Day2001
	• The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person				
RT (309–317)	Pol (476–484 LAI)	ILKEPVHGV	HIV-1 infection	human (A2)	Kelleher2001a
	• Ritonavir (RTV) inhibits chymotryptic activity in the 20S proteasome in vitro, as does Saquinavir (SQV) to a lesser extent; Indinavir (IDV) does not. Thus there is concern protease inhibitors may adversely effect CTL epitope processing, but this paper indicates that processing is not inhibited at therapeutically relevant concentrations of RTV when the proteasome is functioning in in an intracellular context. • RTV did not alter the presentation two RT A2 epitopes processed by distinct pathways: ILKEPVHGV, generated by the constitutive proteasome containing the MB1 beta subunit, and VIYQYMDDL which is dependent on IFNgamma induction of LMP7 which replaces MB1 in the immunoproteasome, and is destroyed by MB1 in the constitutive proteasome. • RTV did not inhibit the processing and assembly of HLA-B35 or -A2, which are assembled with a rapid and moderate time course, respectively, or of HLA-A3, -B27 and -B39.				
RT (309–317)	Pol	ILKDPVHGV	HIV-1 infection	human (A2)	Kaul2002
	• Neisseria gonorrhea cervititis in 9 HIV+ Kenyan sex workers caused a functional deficiency in IFN-gamma production in HIV-1 epitope-specific CD8+ T-cells, detected by intracellular cytokine production and tetramer assays, while not affecting the total number of epitope-specific CTLs. • Ghonorrhea caused the weaker HIV-1 specific CTL responses in 4 HIV-1 exposed persistently seronegative (HEPS) women to become undetectable by Elispot and tetramer assays, and CMV-specific CTL in 2 HEPS subjects were shown to have impaired function with regard to IFN-gamma production.				
RT (309–317)	RT (476–484 NL43)	ILKEPVHGV	HIV-1 infection	human (A2)	Yang2002
	• Nef down-modulates class I protein expression, and this study demonstrates directly that Nef-deleted HIV-1 NL-43 can be more effectively killed in vitro than NL-43 with an intact Nef. The effect was shown to be specific for class I presentation of epitopes, and unlike Nef, deleting Vpr did not alter CTL susceptibility of NL-43 infected cells. The CTL clone 68A62, specific for the class I A2 presented ILKEPVHGV epitope, was one of four used in this study.				
RT (309–317)	RT (476–484 BRU)	ILKEPVHGV	HIV-1 infection	human (A2)	Cohen2002
	• The antigen presentation of two A2-restricted epitopes was compared, SLYNTVATL (p17) and ILKEPVHGV (RT). HIV-1 infected cells were more sensitive to lysis by SLYNTVATL-specific CTL than by ILKEPVHGV-specific CTL, because of a higher density of SLYNTVATL-A2 resulting from differences in processing. • Incubation with a T1-cell proteolytic extract showed that by four hours, 25% of a p17 peptide had a C-term Leu-85 and were SLYNTVATL-precursors, while ILKEPVHGV-precursors were far less frequent (6.8%) even with four times more proteolytic extract after 30 hours. • p17 was preferentially cleaved between Leu85 and Tyr86, while appropriate Val484 and Tyr485 cleavage was minor for RT. • In a competition experiment, RSLYNTVATL bound TAP 3.7-fold more efficiently than RT peptides. • No difference in CTL avidity was detected in six patients with HLA-A2-restricted responses to these epitopes.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• No significant difference in HLA-A2 binding of to p17 or RT epitopes was observed.				
RT (309–317)	Pol (476–484)	ILKEPVHGV	Vaccine	murine (A2)	De Lucca2002
	Vaccine *Vector/Type:* peptide *Adjuvant:* Freund's adjuvant • Epitope name: p9 • BALB/c mice immunized with the p9 peptide, ILKEPVHGV, elicited specific lymphocyte proliferation activity. • Exposure of lymphocytes from HIV-negative, HLA-A2 positive people to p9-RNA stimulated lymphocyte proliferation activity to p9. Anti-p9 CTL activity in human lymphocytes incubated with RNA extracted from lymphoid organs of p9-vaccinated mice could be more intensely stimulated. • This murine RNA also mediated RNA-dependent protein kinase (PKR) and NFkappaB activation in the human lymphocytes, which may be driving the enhanced CTL stimulation in the human cells.				
RT (309–317)	RT	ILKEPVHGV	HIV-1 infection	human (A2)	Oxenius2002b
	• Epitope name: ILK • Using previously defined epitopes [Oxenius2000, Oxenius2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI). • STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.				
RT (309–317)	p51 (476–484)	ILKEPVHGV	Vaccine	murine (A2)	Kmieciak2001
	Vaccine *Strain:* IIIB *HIV component:* Gag, Pol *Adjuvant:* IL-12 (IL-12p35 and IL-12p40) • Transgenic mice expressing a HLA-A2/Kb chimeric protein were vaccinated with either a p17-p24-p51 fusion protein (vG/P-92) or the Gag-Pol precursor protein (vVK1). • Compared to vVK1, vG/P-92 induced a significant increase in Gag and Pol induced IFNgamma production and CTL responses, and to the epitopes SLYNTVATL and ILKEPVHGV, as determined by Elispot and 51Cr-release assays.				
RT (309–317)	Pol (476–484)	ILKEPVHGV	HIV-1 infection	human (A2 supertype)	Propato2001
	• Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus • This epitope can bind three of the five HLA-A2 supertypes alleles (A*0201, A*020 2, A*0203, A*0206 and A*6802)				
RT (309–317)	Pol (464–472)	ILKEPVHGV	HIV-1 infection	human (A2, A*0201)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
RT (309–317)	Pol (subtype B)	ILKEPVHGV	HIV-1 exposed seronegative	human (A2, A*0202)	Rowland-Jones1998b
	• HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes • This epitope is conserved among B and D clade viruses • Clade A version of the epitope, ILKDPVHGV, was preferentially recognized by CTL				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (309–317)	RT (309–317)	ILKEPVHGV	Vaccine, in vitro stimulation	human, murine (A2, A2 transgenic)	De Berardinis2000
	Vaccine *Vector/Type:* HIV-1 peptide in filamentous bacteriophage major coat protein *HIV component:* RT peptides • Epitope name: RT2 • Phage display of the CTL epitope, ILKEPVHGV coupled with T helper epitope KDSWTVNDIQKLVGK, elicited specific CTL responses in vitro in PBMC from HIV negative individuals in and in vivo in immunization of HLA-A2 transgenic mice • Bacteriophage presentation of peptides is generally used for stimulation of antibodies, and this novel discovery of CTL epitope processing and presentation suggests new possibilities for these vectors				
RT (309–317)	Pol	ILKEPVHGV	Vaccine	SJL/J HLA transgenic mice (A2.1)	Ishioka1999
	Vaccine *Vector/Type:* DNA *HIV component:* polyepitope • A minigene vaccine construct encoding 6 HLA 2.1 and 3 HLA A11 restricted CTL epitopes, the universal Th cell epitope PADRE (pan-DR epitope) and an ER translocating signal sequence was constructed • The epitopes were chosen for dominant recognition by CTLs during HBV and HIV infections in humans • HLA transgenic mice were used for quantitating in vivo immunogenicity of DNA vaccines encoding HLA-restricted CTL epitopes – strong responses were observed to all nine epitopes, and CTL memory persisted up to four months after a single injection				
RT (309–317)	RT (476–484 LAI)	ILKEPVHGV	Vaccine	murine (A2.1)	Peter2001
	Vaccine *Vector/Type:* peptide *Strain:* LAI *Adjuvant:* P30, incomplete Freund's adjuvant (IFA), Montanide (ISA 720), PLG-microparticle • Epitope name: LR22 • The stability of peptide binding to HLA-A2.1 was determined for six HLA-A2.1 peptides included in this vaccine study – ILKEPVHGV (RT), SLYNTVATL (p17), SLLNATDIAV (gp41) and LLWKGEGAV (RT) all bound with high affinity comparable to a influenza epitope reference (GILGFVFTL), while RGPGRAFVTI and VIYQYMDDL bound with a lower affinity (relative binding activity = 0.01). • The four high-affinity peptides formed stable complexes with half-lives ranging between 8 and 32 hours, while the low affinity peptides had half lives of less than an hour. • HLA-A2.1 transgenic mice were immunized with the six HIV-1 peptides and P30, as a universal T-helper epitope, with IFA or Montanide or microspheres as adjuvants. • All peptides except VIYQYMDDL induced a stong CTL response in Cr-release assays - stronger responses were observed when peptides were delivered alone, indicating immunodominance when the combination was used.				
RT (309–317)	RT (476–484 LAI)	ILKEPVHGV	Vaccine	murine (A2.1)	Peter2002
	Vaccine *Vector/Type:* peptide *Strain:* LAI *Adjuvant:* P30, incomplete Freund's adjuvant (IFA), IL-12 • Epitope name: LR22 • When HIV-1 peptides were used to vaccinate HLA-A2.1 transgenic A2-Kb mice, strong responses to five peptides were observed when the peptides were given individually, but immunodominance limited the response to some of the peptides when they were given in combination [Peter2001]. IL-12 can counteract immunodominance in BALB/c mice, so it was given with the multiple epitope vaccination, and was instead found to specifically eliminate the HLA-A2.1-epitope CTL responses, but not Kb CTL responses. This was possibly a consequence of transient depletion of T-cells, B cells and macropahges in the spleen.				
RT (309–318)	RT (476–485 LAI)	ILKEPVHGVY	HIV-1 infection	human (B*1501)	Brander2001
	• C. Brander notes this is a B*1501 epitope				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (309–318)	RT (309–318)	IKLEPVHGVY	HIV-1 infection	human (B62)	Day2001
	• No immunodominant responses were detected to four B62-restricted epitopes tested				
RT (309–318)	RT (476–485 LAI)	ILKEPVHGVY	HIV-1 infection	human (Bw62)	McMichael1994, Menendez-Arias1998
	• Review of HIV CTL epitopes				
RT (309–318)	Pol	ILKEPVHGVY	HIV-1 infection, Vaccine	human (Bw62)	Hanke2000, Wee2002
	Vaccine *Vector/Type:* DNA prime with vaccinia MVA boost *Strain:* subtype A *HIV component:* p17, p24, polyepitope				
	• The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000].				
	• Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].				
RT (328–352)	RT (495–515 LAI)	EIQKQGQGQWTYQIYQEPF-KNLKTG	HIV-1 infection	human (A11)	Menendez-Arias1998, Walker1989
	• One of five epitopes defined for RT-specific CTL clones in this study				
RT (340–350)	RT (507–516)	QIYQEPFKNLK	HIV-1 infection	human	Menendez-Arias1998, Price1995
	• Study of cytokines released by HIV-1 specific activated CTL				
RT (340–350)	Pol (487–497 93TH253 subtype CRF01)	QIYQEPFKNLK	HIV-1 infection, HIV-1 exposed seronegative	human (A11)	Sriwanthana2001
	• Epitope name: P495-505				
	• This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand				
	• HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed				
	• This epitope was weakly reactive in the HEPS study subject 128 who was HLA A11/A33				
	• This epitope was reactive in HIV+ study subjects 053 and 184 who carried HLA-A11				
RT (340–350)	Pol (487–497 93TH253 subtype CRF01)	QIYQEPFKNLK	HIV-1 infection	human (A11)	Bond2001
	• HLA-A11 CRF01 (called subtype E in Bond et al.) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive				
	• 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 finding and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified				
	• This epitope was not predicted by the EpiMatrix method to be likely to bind to A11, though it served as an epitope in the FSWs, and it was one of the six A11 epitopes that had been previously defined				
	• 5/8 tested FSWs recognized this epitope				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This epitope was highly conserved in other subtypes, although exact matches were not very common				
RT (340–352)	RT (507–519 LAI)	QIYQEPFKNLKTG	HIV-1 infection	human (A11)	Johnson1994c, Menendez-Arias1998
	• This epitope was listed in a review				
RT (340–352)	Pol (495–507)	QIYQEPFKNLKTG	HIV-1 infection	human (A11)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
RT (341–350)	RT (508–516)	IYQEPFKNLK	HIV-1 infection	human (A*1101)	Culmann1998
	• C. Brander notes that this is an A*1101 epitope in the 1999 database				
RT (341–350)	RT (508–517 LAI)	IYQEPFKNLK	HIV-1 infection	human (A*1101)	Brander2001
	• C. Brander notes this is an A*1101 epitope				
RT (341–350)	RT (508–517 SF2)	IYQEPFKNLK	HIV-1 infection	human (A11)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-A11+ individuals that had a CTL response to this epitope broken down by group: 0/3 group 1, 0/0 group 2, and 1/2 group 3				
RT (341–350)	Pol (508–516)	IYQEPFKNLK	HIV-1 infection, HIV-1 exposed seronegative	human (A11)	Kaul2001a
	• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers				
RT (356–365)		RMRGAHTNDV	HIV-1 infection	human (A*3002)	Sabbaj2002b
	• Epitope name: Pol-RV10 • This study monitored epitope responses in HIV-1 infected minority women living in the United States • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release • Subject 01RCH50 also recognized the epitope WRFDSRLAF, Nef(183-191), B*1503 • Among HIV+ individuals who carried HLA A30, 5/16 (31%) recognized this epitope				
RT (356–366)	RT (15–26)	RMRGAHTNDVK	HIV-1 infection	human (A3)	Yu2002a
	• Epitope name: A3-RK11 • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• 0/14 HLA-A3 positive individuals had detectable A3-restricted responses to this epitope during acute infection, but only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 5/7 individuals began to have detectable responses to this epitope after STI.				
RT (364–372)	RT (518–526 U455)	DVKQLTEVV		human (A28, A*6802)	Dong1998a, Menendez-Arias1998
	• Predicted on binding motif, no truncations analyzed • Reacts with clade A consensus (U455), and with the peptide DVKQLAEAV, from the D clade				
RT (364–372)	RT (470–478 subtype A)	DVKQLTEVV	HIV-1 infection	human (B70)	Dorrell1999
	• CTL responses in three individuals with non-clade B infections were studied, 2 with subtype A infections, 1 with subtype C – their infections all originated in East Africa • This CTL response was defined in a patient with an A subtype infection • Bulk cultures from this patient gave a CTL response that could recognize the subtype D form of this epitope, with two substitutions (DVKQLAEAV), though a CTL line from these cultures didn't recognize the B clade variant (DVKQLTEAV)				
RT (366–385)	Pol (521–540)	KQLTEAVOKIAMESIVIWGK	HIV-1 infection	human	Novitsky2002
	• HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
RT (374–383)	RT (LAI)	KITTESIVIW	HIV-1 infection	human (B*5701)	Menendez-Arias1998, vanderBurg1997
	• Patients studied were from the Amsterdam cohort • CTL epitopes of 3 rapid progressors were compared to 4 long-term survivors (LTS); no differences could be found in the degree of conservation between them • Epitope recognized by LTS and by a progressor				
RT (374–383)	RT (LAI)	KITTESIVIW	HIV-1 infection	human (B*5701)	vanderBurg1997
	• Recognized by CTL from a progressor and a long-term survivor, PIVLPEKDSW was also recognized				
RT (375–383)	RT (375–383 LAI)	ITTESIVIW	HIV-1 infection	human (B*5701 B*5801)	Klein1998
	• Another patient recognized the ten-mer version of this epitope, KITTESIVIW [vanderBurg1997] • B57 has been associated with long-term non-progression in the Amsterdam cohort • The most pronounced CTL responses in HLA B*5701 LTS were to RT and Gag • The patient that recognized ITTESIVIW also recognized IVLPEKDSW				
RT (375–383)	RT (375–383 SF2)	ITTESIVIW	HIV-1 infection	human (B57)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Number of HLA-B57+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 0/0 group 2, and 1/2 group 3				
RT (392–401)	RT (559–568 LAI)	PIQKETWETW		human (A*3201)	Harrer1996b, Menendez-Arias1998
	• Reviewed in [Menendez-Arias1998], suggest the epitope is HLA B53/Cw2 • C. Brander notes that this is an A*3201 epitope in the 1999 database				
RT (392–401)	RT (559–568 LAI)	PIQKETWETW		human (A*3201)	Brander2001
	• C. Brander notes this is an A*3201 epitope				
RT (392–401)		PIQKETWETW	HIV-1 infection	human (A*3201)	Sabbaj2002b
	• Epitope name: Pol-PW10 • This study monitored epitope responses in HIV-1 infected minority women living in the United • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previou • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated • Subject 01RCH59 was Hispanic, was not on HAART, viral load 5100, CD4 count 349, and she also recognized QASQEVKNW, p24(176-184), B*5301 • Among HIV+ individuals who carried HLA A32, 1/2 (50%) recognized this epitope				
RT (392–401)	RT (559–568 SF2)	PIQKETWETW	HIV-1 infection	human (A32)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-A32+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 1/1 group 2, and 0/0 group 3				
RT (392–401)	RT	PIQKETWETW	HIV-1 infection	human (A32)	Altfeld2002
	• Epitope name: A32-PW10(RT) • Peripheral blood (PB) and lymph node (LN) CD8+ T-cell responses were compared in 15 asymptomatic HIV-1 infected patients using all known optimal CTL epitopes (http://hiv-web.lanl.gov/content/hiv-db/REVIEWS/brander2001.html) for each person's class I HLA alleles. • 60 epitope responses were detected in both PB and LN samples of the 15 patients, and an additional 8 responses were detected only in LN. The total magnitude of the response was similar in LN and PB, but the percentage of CD8+ T cells in the LN is lower so the number of HIV-specific cells per million CD8+ T-cells is higher in the LN. • 1 year post-HAART treatment in five patients studied, the magnitude of the CD8 T-cell response was decreased in both LN and PB, but more dramatically in PB, and 13/25 epitope responses in the PB became undetectable, in contrast to 5/26 in the LN. • Treatment interruption following HAART induced resulted in increased viremia accompanied by the restoration of the detection of 13 epitopes that had become undetectable in the PB, and the addition of 9 novel epitope responses. • Breakdowns of epitope responses were shown for 4 individuals. Patient A displayed the greatest response to epitope B14-EL9(gp41), a strong response to B7-TL9(p24), and responses to B7-TM9(Nef) and A32-PW10(RT). Patient B displayed the greatest response to epitope B44-AW11(p24) and also responded to A32-PW10(RT) in both PB and LN samples, while a third response against epitope A32-RW10(gp120) was only detected in the LN sample. Patient D displayed the greatest response to B27-KK10 (p24), and also responded to A30-RY11(p17), A32-PW10(RT), A30-KY11(RT), A32-RW10(gp120), and B18-YY9(Nef).				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (397–406)	RT (LAI)	TWETWWTEYW	HIV-1 infection	human (B44)	Menendez-Arias1998, vanderBurg1997
	• Recognized by CTL from two progressors, EILKEPVGHGV and EELRQHLLRW were also recognized by one, and RETKLGKAGY was also recognized by the other				
RT (416–424)	Pol (563–571 93TH253 subtype CRF01)	FVNTPPLVK	HIV-1 exposed seronegative	human (A11)	Sriwanthana2001
	• Epitope name: P571-579 • This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand • HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed • This epitope was weakly reactive in the HEPS study subject 128 who was HLA A11/A33				
RT (416–424)	Pol (563–571 93TH253 subtype CRF01)	FVNTPPLVK	HIV-1 infection	human (A11)	Bond2001
	• HLA-A11 CRF01 (called subtype E in Bond et al.) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive • 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 finding and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified • This is one of the new A11 epitopes identified through the streamlined EpiMatrix method, and 1/8 tested FSWs recognized it • This epitope was conserved many subtypes (but not subtype H), but exact matches were not very common				
RT (421–429)	RT (421–429)	PLVKLWYQL	HIV-1 infection	human (A2)	Haas1998
	• Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively) • New clusters of epitopes were defined utilizing different HLA molecules				
RT (432–440)	RT (587–597 SF2)	EPIVGAETF	HIV-1 infection	human (B*3501)	Menendez-Arias1998, Tomiyama1997
	• A CTL clone responsive to this epitope was obtained • 5/7 B35-positive individuals had a CTL response to this epitope • An E to D substitution at position 1, and V to I at position 4, reduces activity but not binding to B*3501 • [Menendez-Arias1998] note in their review that this epitope is near the protease cleavage site and conservation of this region is important for proper viral maturation				
RT (432–440)	Pol (587–595)	EPIVGAETF	HIV-1 infection	human (B*3501)	Tomiyama2000a
	• CD8+ T-cells that bound one of six HIV-specific B*3501-epitope tetramers did not express CD28 or CD45A • A significant increase in CD28-CD45RA- cells and a decrease of CD28+CD45RA+ cells was observed in chronically HIV-1-infected individuals relative to healthy individuals • CD28-CD45RA- cells are likely to be effector cells and have high levels of perforin in their cytoplasm • The mean percentage of total CD28- CD8+ cells in chronically infected HIV-1-infected patients was 76.6% in comparison to HIV-1-uninfected individuals (40.6%)				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (432–440)		EPIVGAETF	HIV-1 infection	human (B35)	Wilson2000a
• Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load was also found • All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39 • ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK • The subject with A*0201 had a moderatly strong response to SLYNTVATL • Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705 • No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL			
RT (432–440)	Pol (587–595)	EPIVGAETF	HIV-1 infection	human (B35)	Dyer1999
• CTL specific responses were measured over a 1.3 to 1.5 year period in members of the Sydney Blood Bank Cohort (SBBC) who had been infected with a natural attenuated strain of HIV-1 which was Nef-defective • Some of these patients had prolonged high levels of CTL effector and memory cells despite low viral load					
RT (432–440)	RT (587–596 SF2)	EPIVGAETF	HIV-1 infection	human (B35, B51)	Shiga1996
• Binds HLA-B*3501, and is also presented by B51 – but CTL could not kill RT-vaccinia virus infected cells that expressed B51					
RT (432–440)	Pol (587–595)	EPIVGAETF	HIV-1 infection	human (B35, B51)	Ferrari2000
• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles					
RT (432–441)	Pol (587–596)	EPIVGAETFY	HIV-1 infection	human (B*3501)	Tomiyama2000a
• CD8+ T-cells that bound one of six HIV-specific B*3501-epitope tetramers did not express CD28 or CD45A • A significant increase in CD28-CD45RA- cells and a decrease of CD28+CD45RA+ cells was observed in chronically HIV-1-infected individuals relative to healthy individuals • CD28-CD45RA- cells are likely to be effector cells and have high levels of perforin in their cytoplasm • The mean percentage of total CD28- CD8+ cells in chronically infected HIV-1-infected patients was 76.6% in comparison to HIV-1-uninfected individuals (40.6%)					
RT (432–441)	RT (587–597 SF2)	EPIVGAETFY	HIV-1 infection	C3H/HeJ mice (B35)	Menendez-Arias1998, Shiga1996
• Binds HLA-B*3501, but not presented by B51, in contrast to the peptide EPIVGAETF • [Menendez-Arias1998] note in their review that this epitope is located near the protease cleavage site and conservation of this region is important for viral maturation • This epitope spans the Pol p66 RT – p15 (RNAse) domain					
RT (432–441)	RT (587–597 SF2)	EPIVGAETFY	HIV-1 infection	human (B35)	Kawana1999
• HLA B35 is associated with rapid disease progression • The sequences of 9 previously described HIV-1 B35 CTL epitopes were obtained in 10 HLA B35+ and 19 HLA B35- individuals					

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• 3/9 CTL epitopes had substitutions that were more common in B35+ individuals than in B35- individuals, but this was one of the six that had no B35 associated pattern of mutation				
RT (434–447)	RT (LAI)	IVGAETFYVDGAAS	HIV-1 infection	human (A*6802)	Menendez-Arias1998, vanderBurg1997
	• Recognized by CTL from a long-term survivor that recognized a set of 5 overlapping peptides spanning IVGAETFYVDGAAS as well as PIVLPEKDSW and KITTESIVIW • A*6802 is a subset of HLA-A28 • This epitope spans the Pol p66 RT – p15 (RNAse) domain				
RT (436–445)	RT (591–600 IIIB)	GAETFYVDGA	HIV-1 infection	human (B45)	Menendez-Arias1998
	• This epitope spans the Pol p66 RT – p15 (RNAse) domain				
RT (436–445)	Pol (591–600 IIIB)	GVETFYVDGA	HIV-1 infection	human (B45)	Wilson1999a
	• This study describes maternal CTL responses in the context of mother-to-infant transmission • Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants • No variants of this epitope were found in a non-transmitting mother who had a CTL response to it • This epitope spans the Pol p66 RT – p15 (RNAse) domain				
RT (437–445)		AETFYVDGA	HIV-1 infection	human (B*4501)	Sabbaj2002b
	• Epitope name: Pol-AA9 • This study monitored epitope responses in HIV-1 infected minority women living in the United States • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release • Subject 00RCH33 was on HAART had a viral load of 2900 and CD4 count of 727 and also recognized the epitopes YPLTFGWCY, Nef(135-143), HLA B*5301; RSLYNTVATLY, p17(76-86), HLA A*3002; and HIGPGRAFY, gp160(310-318), HLA A*3002 • Among HIV+ individuals who carried HLA B45, 3/9 (33%) recognized this epitope				
RT (437–447)	RT (592–602 LAI)	AETFYVDGAAN		human (A28)	Brander1996b, Menendez-Arias1998
	• P. Johnson, pers. comm. • This epitope spans the Pol p66 RT – p15 (RNAse) domain				
RT (437–447)	Pol (592–602)	AETFYVDGAAN	HIV-1 infection	human (A28)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
RT (438–448)	RT (593–603 IIIB)	ETFYVDGAANR	HIV-1 infection	human (A26)	Menendez-Arias1998
	• This epitope spans the Pol p66 RT – p15 (RNAse) domain				
RT (438–448)	Pol (593–603 IIIB)	ETFYVDGAANR	HIV-1 infection	human (A26)	Wilson1999a
	• This study describes maternal CTL responses in the context of mother-to-infant transmission • Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants • One other variant was found that gave a positive, though reduced, CTL response: ETYYVNGAANR				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This epitope spans the Pol p66 RT – p15 (RNAse) domain				
RT (448–457)	RT	RETKLGKAGY	HIV-1 infection	human (A29)	vanderBurg1997
	• Patients studied were from the Amsterdam cohort • CTL epitopes of 3 rapid progressors were compared to 4 long-term survivors (LTS) and no differences could be found in the degree of conservation between them • Epitope recognized by a LTS • This epitope occurs in the p15 (RNAse) domain of Pol p66 RT				
RT (449–457)		ETKLGKAGY	HIV-1 infection	human (A*2601)	Sabbaj2002b
	• Epitope name: Pol-EY9 • This study monitored epitope responses in HIV-1 infected minority women living in the United States • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release • Subject 03RCH40 was African American, had a viral load of 2500, CD4 count of 372, was not on HAART, and also recognized the epitope DILDLWIY, Nef(108-115), HLA Cw*0701 • Among HIV+ individuals who carried HLA A26, 2/8 (25%) recognized this epitope				
RT (481–505)	RT (648–672)	AIYLALQDSGLEVNIVTDS-QYALGI	HIV-1 infection	human	Menendez-Arias1998, Price1995
	• Study of cytokines released by HIV-1 specific activated CTL • This epitope occurs in the p15 (RNAse) domain of Pol p66 RT				
RT (481–505)	RT (648–672 PV22)	AIYLALQDSGLEVNIVTDS-QYALGI	HIV-1 infection	human (B14)	Kalams1994, Menendez-Arias1998
	• A CTL response used to study gene usage in HLA-B14 response • This epitope occurs in the p15 (RNAse) domain of Pol p66 RT				
RT (485–493)	Pol (649–659 BH10, LAI)	ALQDSGLEV	HIV-1 infection	human	Maksiutov2002
	• This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins. • This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is IYLALQDSGLE) has similarity with the epidermal growth factor receptor kinase substrate EPS8, fragment ISAAASDSGVE.				
RT (485–493)	RT (640–648 HXB2R) **Vaccine** *Strain:* HXB2 *HIV component:* RT	ALQDSGLEV	Vaccine	human (A2)	Brander1995a
	• Epitope studied in the context of inclusion in a synthetic vaccine • This epitope occurs in the p15 (RNAse) domain of Pol p66 RT				
RT (485–493)	RT (640–648 HXB2R)	ALQDSGLEV	HIV-1 infection	human (A2.1)	Brander1995a, Brander1996a
	• This epitope was recognized by PBMC from 3/14 HIV+ asymptomatic patients • This epitope was used along with Env CTL epitope TLTSCNTSV and a tetanus toxin T helper epitope for a synthetic vaccine • This vaccine failed to induce a CTL response, although a helper response was evident • This epitope occurs in the p15 (RNAse) domain of Pol p66 RT				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (485–505)	RT (648–672)	ALQDSGLEVVTDSQYALGI	HIV-1 infection	human (B14)	Brander1995b
	• Unpublished, S. Kalams • This epitope occurs in the p15 (RNAse) domain of Pol p66 RT				
RT (496–505)		VTDSQYALGI	HIV-1 infection	human (B*1503)	Sabbaj2002b
	• Epitope name: Pol-VI10 • This study monitored epitope responses in HIV-1 infected minority women living in the United States • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release • Subject 01RCH51 was an African American on HAART, viral load 980, CD4 count 811 • Among HIV+ individuals who carried HLA B15, 1/17 (6%) recognized this epitope				
RT (496–505)	Pol (subtype B)	VTDSQYALGI	HIV-1 exposed seronegative	human (B14, B*1402)	Rowland-Jones1998b
	• HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes • This epitope is conserved among A, B and D clade viruses				
RT (496–505)	RT (663–672 IIIB)	VTDSQYALGI	HIV-1 infection	human (Cw8)	Brander1996b
	• Unpublished, P. Johnson • Published in this database in 1995 as B14, but B14 transfected cells did not present the peptide and it is thought to be presented by the genetically linked Cw8 molecule instead [Brander1996b] • This epitope occurs in the p15 (RNAse) domain of Pol p66 RT				
RT (496–505)	RT	VTDSQYALGI	HIV-1 exposed seronegative	human (Cw8)	Rowland-Jones1998a
	• A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating • The A and D subtype consensus are identical to the B clade epitope • Thought to be HLA-Cw8 restricted, not B14 as originally reported (C. Brander, B. Walker, and S. Rowland-Jones, personal communication) • This epitope occurs in the p15 (RNAse) domain of Pol p66 RT				
RT (509–518)	Pol	QPDKSESELV		human (B7)	De Groot2001
	• The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes • A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes were identified that could stimulate IFNγ production in an ELISPOT assay • QPDKSESELV was newly identified as an HLA-B7 epitope in this study				
RT (516–525)	RT (516–525)	ELVNQIIEQL	HIV-1 infection	human (A2)	Haas1998
	• Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively) • New clusters of epitopes were defined utilizing different HLA molecules • This epitope occurs in the p15 (RNAse) domain of Pol p66 RT				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (520–528)	Pol (520–528 LAI) • C. Brander notes this is an A*1101 epitope	QIIEQLIKK		human (A*1101)	Brander2001, Fukada1999
RT (520–528)	Pol (675–683) • Counterparts for eight known clade B HLA A*1101 epitopes were generated for clade E (CRF01). Three epitopes, identical among clade A-E, were cross-reactive and recognized by clade E infected individuals. The clade E and B analogs to three more HLA A*1101 epitopes was recognized in a clade specific manner. Two other HLA A*1101 clade B defined epitopes were found not to have stimulated a response in clade E infected individuals. • QIIEQLIKK was found to elicit clade-specific responses in clade B (QIIEQLIKK is most common) and clade E (qiieElikk is most common). QIIEQLIKK was strongly recognized by CTL from 1/5 B clade infected Japanese subjects, and qiieElikk from 3/7 E clade infected Thai subjects. The variant qiieKliEk, common in the A subtype, was also recognized in 2/7 E clade infected Thai subjects. • The binding of QIIEQLIKK, qiieElikk and qiieKliEk to HLA A*1101 was similar, but CTL clones from individuals did not cross-react with the cross-clade peptides indicating that the substitutions inhibited TCR interaction.	QIIEQLIKK	HIV-1 infection	human (A*1101)	Fukada2002
RT (530–538)	Pol (680–691 BH10, LAI) • This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins. • This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is IKKEKVYLAWV) has similarity with B-cell growth factor precursor, fragment IKKERLWLGPV.	KVYLAWVPA	HIV-1 infection	human	Maksiutov2002
RT (530–538)	• Epitope name: Pol-KA9 • This study monitored epitope responses in HIV-1 infected minority women living in the United States • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release • This epitope was newly defined in this study • Patient 04RCH86 was Hispanic, not on HAART, and had a viral load of 7600 and CD4 count of i774 • Among HIV+ individuals who carried HLA A*03, 2/21 (10%) recognized this epitope	KVYLAWVPA	HIV-1 infection	human (A*0301)	Sabbaj2002b
RT (532–540)	Pol (714–722) • Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus • This epitope can bind 5/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801)	YLAWVPAHK	HIV-1 infection	human (A3 supertype)	Propato2001
RT (532–540)	RT (532–540) • Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively) • New clusters of epitopes were defined utilizing different HLA molecules • This epitope occurs in the p15 (RNAse) domain of Pol p66 RT	YLAWVPAHK	HIV-1 infection	human (B7)	Haas1998

II-B-11 Integrase CTL Epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Integrase (20–28)	Pol (762–770)	RAMASDFNL	HIV-1 infection	human (A2 supertype)	Propato2001
	• Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus • This epitope can bind three of the five HLA-A2 supertypes alleles (A*0201, A*020 2, A*0203, A*0206 and A*6802)				
Integrase (22–31)	Pol (764–773)	MASDFNLPPV	HIV-1 infection	human (A2 supertype)	Propato2001
	• Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus • This epitope can bind all five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802)				
Integrase (28–36)	Pol (743–751 SF2)	LPPVVAKEI	HIV-1 infection	human (B*5101)	Tomiyama1999
	• HLA-B27, -B51, and -B57 are associated with slow progression to AIDS, while HLA-B35, -B8, -B24 are associated with a rapid progression to AIDS (Nat. Med. 2:405, 1996;Lancet 22:1187, 1986;Hum Immunol 22:73, 1988;Hum Immunol 44:156, 1995) • 15% of Japanese populations carry HLA-B51 while HLA-B27 and -B57 are detected in less than 0.3% • Of the 172 HIV-1 peptides with HLA-B*5101 anchor residues, 33 bound to HLA-B*5101, seven of these peptides were reactive with CTL from 3 B*5101 positive individuals, and six were properly processed • Four of the six epitopes were highly conserved among B subtype sequences – LPPVVAKEI is highly conserved				
Integrase (82–89)	RT (797–804 SF2)	GYIEAEVI	HIV-1 infection	human (A*2402)	Ikeda-Moore1997
	• Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402 • This peptide induced CTL in 1/4 HIV-1+ people tested • GYIEAEVI bound to A*2402 weakly, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained				
Integrase (89–98)	Pol (805–814 BH10, LAI)	IPAETGQETA	HIV-1 infection	human	Maksiutov2002
	• This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins. • This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is PAETGQETAY) has similarity with Integrin beta-4 precursor (GP150)(CD104), fragment PAETNGEITAY.				
Integrase (89–98)	Pol	IPAETGQETA		human (B56)	De Groot2001
	• The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes • A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes could stimulate IFNγ production in an ELISPOT assay • IPAETGQETA was newly identified as an HLA-B56 epitope in this study				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Integrase (96–104)	Integrase (823–831)	ETAYFILKL		human (A*6802)	Dong1998b
	• Epitope found in clade A, B, and D – Pers. Comm. S. Rowland-Jones and T. Dong				
Integrase (96–104)	Pol (subtype A)	ETAYFILKL	HIV-1 exposed seronegative	human (A*6802)	Kaul2000
	• 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 gamma-IFN responses in the cervix – systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses • Low risk individuals did not have such CD8+ cells • CD8+ T cell epitopes: DTVLEDINL (3 individuals), SLYNVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women				
Integrase (96–104)	Pol	ETAYFILKL	HIV-1 infection	human (A*6802)	Kaul2001c
	• This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative • The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire • This epitope was recognized in 1/22 HEPS sex worker controls (ML1671)				
Integrase (96–104)	Pol (744–752)	ETAYFYILKL	HIV-1 infection, HIV-1 exposed seronegative	human (A*6802)	Kaul2001a
	• ETAYFYILKL cross-reacts with clades A, B and D • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure • Among HLA-A*6802 women, 3/12 HEPS and 9/11 HIV-1 infected women recognized this epitope likelihood ratio 7.9, p value 0.01, and HEPS women tended to respond to DTVLEDINL, while infected women to ETAYFYILKL • The dominant response to this HLA allele was to this epitope in 2 of the 3/12 HEPS cases and in all 9/11 HIV-1 infected women that responded to the epitope • Differences in epitope specificity were only seen for responses restricted by class I HLA alleles A2, A24, A*6802, B14, and B18, previously shown to be associated with resistance to HIV-1 in this cohort • Subject ML 1203 started with CTL responses to A*6802 DTVLEDINL and to B7 FPVTPQVPLR prior to seroconversion, and upon seroconversion acquired additional responses to A*6802 ETAYFILKL which became dominant, B7 TPGPG(V/I)RYPL, B7 IPRRIRQGL, and B7 SPRTLNAWV • Subject ML 1707 started with a CTL response to A*6802 DTVLEDINL prior to seroconversion, and switched to A*6802 ETAYFILKL and A24 RDYVDRFFKTL post-seroconversion • Subject ML 1830 made no detectable response prior to seroconversion, but responded to A*6802 DTVLEDINL and A*6802 ETAYFILKL post-seroconversion				
Integrase (96–104)	Pol (744–752)	ETAYFILKL	HIV-1 infection	human (A*6802)	Appay2000
	• This epitope is newly defined in this study • Combined tetramer and intracellular cytokine staining was used to study the function of circulating CD8+ T cells specific for HIV and CMV • HIV-specific CD8+ T cells expressed lower levels of perforin than CMV-specific CD8+ T cells from the same donor, and this was associated with persistent CD27 expression on HIV-specific cells, suggesting impaired maturation				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• In most donors, between 50% and 95% of the activated virus-specific CD8+ T cells produced IFN-γ and MIP-1β with a distinct subset that failed to produce TNF-α				
Integrase (127–135)	Pol (869–877)	KAACWWAGI	HIV-1 infection	human (A2 supertype)	Propato2001
	• Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus • This epitope can bind three of the five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802)				
Integrase (173–181)	Pol (888–896)	KTAVQMAVF		human (B*5701)	Brander2001
	• C. Brander notes this is a B*5701 epitope • Epitope is motif based, personal communication from C. Hay • Subtype of B57 not determined				
Integrase (173–181)	Pol (888–896)	KTAVQMAVF		human (B57)	Hay1999a
	• Epitope is motif based, personal communication from C. Hay				
Integrase (177–186)	Pol (919–928)	QMAVFIHNFK	HIV-1 infection	human (A3 supertype)	Propato2001
	• Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus • This epitope can bind 5/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801)				
Integrase (178–186)	Pol (920–928)	MAVFIHNFK	HIV-1 infection	human (A3 supertype)	Propato2001
	• Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus • This epitope can bind 3/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801)				
Integrase (179–187)	Pol (921–929)	AVFIHNFKR	HIV-1 infection	human (A3 supertype)	Propato2001
	• Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus • This epitope can bind 5/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801)				
Integrase (179–188)	Integrase (179–188 LAI)	AVFIHNFKRK		human (A*1101)	Brander2001, Fukada1999
	• C. Brander notes this is an A*1101 epitope				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Integrase (179–188)	Pol (894–903)	AVFIHNFKRK	HIV-1 infection	human (A*1101)	Fukada2002
	• Counterparts for eight known clade B HLA A*1101 epitopes were generated for clade E (CRF01). Three epitopes, identical among clade A-E, were cross-reactive and recognized by clade E infected individuals. The clade E and B analogs to three more HLA A*1101 epitopes was recognized in a clade specific manner. Two other HLA A*1101 clade B defined epitopes were found not to have stimulated a response in clade E infected individuals. • AVFIHNFKRK is commonly found in viruses representing subtypes A-E. It was strongly recognized by CTL from 4/7 E clade infected Thai subjects.				
Integrase (179–188)	Pol (894–903 93TH253 subtype CRF01)	AVFIHNFKRK	HIV-1 exposed seronegative	human (A11)	Bond2001
	• Epitope name: P894-903 • This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand • HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed • This epitope was weakly reactive in the HEPS study subjects 265 who was HLA A2/A11 and 128 who was HLA A11/A33, and had been predicted to be a possible A11 epitope using Epimer in [Bond2001]				
Integrase (179–188)	Int (894–904)	AVFIHNFKRK	HIV-1 infection	human (A3)	Yu2002a
	• Epitope name: A3-AK10 • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 0/14 HLA-A3 positive individuals had detectable A3-restricted responses to this epitope during acute infection, but only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 1/7 individuals began to have detectable responses to this epitope after STI.				
Integrase (179–196)	Pol (894–911)	AVFIHNFKRKGGIGGYSA	HIV-1 infection	human	Novitsky2002
	• HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
Integrase (210–227)	Pol (925–942)	TKELQKQIIKIQNFRVYY	HIV-1 infection	human	Novitsky2002
	• HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
Integrase (219–227)		KIQNFRVYY	HIV-1 infection	human (A*3002)	Sabbaj2002b
	• Epitope name: Pol-KY9 • This study monitored epitope responses in HIV-1 infected minority women living in the United States • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release • Patient 00RCH28 was African American, not on HAART, had a viral load of 5900 and CD4 count of 889, and she also recognized RIRQGLERA, gp160(846-854), A*0205				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Among HIV+ individuals who carried HLA A30, 6/16 (38%) recognized this epitope				
Integrase (219–228)	Pol (919–928)	KIQNFRVYYR	HIV-1 infection	human (A3 supertype)	Propato2001
	• Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus • This epitope can bind 5/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801)				
Integrase (241–249)	Pol (576–584)	LLWKGEGAV	in vitro stimulation	human (A*0201)	vanderBurg1996
	• Slow dissociation rate, associated with immunogenicity in transgenic HLA-A*0201/K^b mice • CTL generated by in vitro stimulation of PBMC derived from uninfected individual				
Integrase (241–249)	Pol (956–964)	LLWKGEGAV	HIV-1 infection	human (A2)	Kundu1998b
	• Allogeneic dendritic cells (DCs) were obtained from HLA-identical siblings, pulsed with rgp160 MN or A2-restricted HIV-1 epitope peptides, and infused monthly into six HIV-infected patients • 1/6 showed increased Env-specific CTL and increased lymphoproliferative responses, 2/6 showed increase only in proliferative responses, and 3/6 showed no change – pulsed DCs were well tolerated • LLWKGEGAV is a conserved HLA-A2 epitope included in this study – 6/6 patients had this sequence as their HIV direct sequence, but only four of these had a detectable CTL response				
Integrase (241–249)	Pol (956–964 HXB2R)	LLWKGEGAV	Peptide-HLA interaction	human (A2)	Parker1992, Parker1994
	• Studied in the context of HLA-A2 peptide binding				
Integrase (241–249)	Pol (956–964 HXB2R)	LLWKGEGAV	Peptide-HLA interaction	human (A2)	Brander1995a
	• No CTL activity found in HIV-infected subjects, epitope studied in the context of inclusion in a synthetic vaccine				
Integrase (241–249)	Pol (956–964)	LLWKGEGAW	HIV-1 infection	human (A2, A*0201)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
Integrase (241–249)	RT (956–964 HXB2R)	LLWKGEGAV	Vaccine	murine (A2.1)	Peter2001
	Vaccine *Vector/Type:* peptide *Strain:* LAI *Adjuvant:* P30, incomplete Freund's adjuvant (IFA), Montanide (ISA 720), PLG-microparticle • Epitope name: LR28 • The stability of peptide binding to HLA-A2.1 was determined for six HLA-A2.1 peptides included in this vaccine study – ILKEPVHGV (RT), SLYNTVATL (p17), SLLNATDIAV (gp41) and LLWKGEGAV (RT) all bound with high affinity comparable to a influenza epitope reference (GILGFVFTL), while RGPGRAFVTI and VIYQYMDDL bound with a lower affinity (relative binding activity = 0.01). • The four high-affinity peptides formed stable complexes with half-lives ranging between 8 and 32 hours, while the low affinity peptides had half lives of less than an hour. • HLA-A2.1 transgenic mice were immunized with the six HIV-1 peptides and P30, as a universal T-helper epitope, with IFA or Montanide or microspheres as adjuvants. • All peptides except VIYQYMDDL induced a stong CTL response in Cr-release assays - stronger responses were observed when peptides were delivered alone, indicating immunodominance when the combination was used.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Integrase (241–249)	RT (956–964 HXB2R)	LLWKGEGAV	Vaccine	murine (A2.1)	Peter2002

Vaccine *Vector/Type:* peptide *Strain:* LAI *Adjuvant:* P30, incomplete Freund's adjuvant (IFA), IL-12

- Epitope name: LR28
- When HIV-1 peptides were used to vaccinate HLA-A2.1 transgenic A2-Kb mice, strong responses to five peptides were observed when the peptides were given individually, but immunodominance limited the response to some of the peptides when they were given in combination [Peter2001]. IL-12 can counteract immunodominance in BALB/c mice, so it was given with the multiple epitope vaccination, and was instead found to specifically eliminate the HLA-A2.1-epitope CTL responses, but not Kb CTL responses. This was possibly a consequence of transient depletion of T-cells, B cells and macropahges in the spleen.

II-B-12 Pol CTL Epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Pol	RT (LAI)		HIV-1 infection	human	Buseyne1998a
	• This study showed a correlation between strong CTL memory and breadth of response in 7-12 month old infants, and remaining AIDS-free for the first year of life, higher absolute CD4 and CD8 cells, and lower viral load				
Pol	p66 (LAV)		HIV-1 infection	human	Zheng1999
	• Protein delivery (gp160 LAV, p66 LAV, and p24 NY5) to human dendritic cells (DC) with liposomes provides enhanced memory CTL response relative to delivery of protein alone • Chloroquine administration enhanced epitope presentation, and brefeldin A and peptide aldehyde inhibitors inhibited antigen presentation, suggesting epitopes were processed by classical proteasome pathway				
Pol	Pol (IIIB)		HIV-1 infection	human	Wasik2000
	• HIV+ infants that progressed rapidly to AIDS had lower Th1 responses and decreased production of beta-chemokines and IL-2 relative to other HIV+ infants • No HIV+ infants had no demonstrable CTL at birth, but Th1 responses accompanied by CTL responses developed in children with slowly progressive disease, and not in rapid progressors • CTLp frequencies were determined by limiting dilution using autologous B cells infected with vaccina/HIV constructs				
Pol	Pol (LAI)		Vaccine	human	Salmon-Ceron1999
	Vaccine *Vector/Type:* canarypox *Strain:* LAI, MN *HIV component:* gp41, Gag, Pro, V3 • The vaccine used was a rec canarypox with HIV-1 gp120 MN, tm/gag/protease LAI (vCP205), alone or with p24E-V3 MN synthetic peptide (CLTB-36)) • Twenty HIV negative subjects were vaccinated in phase I trial with combinations of vCP205 and CLTB-36 • Immunization with vCP205 induced HIV-1-specific ABs to gp120, V3, and p24 antigens, and CTL immune responses against vCP205 were detected after the fourth immunization in 33% of the subjects against Env, Gag and Pol, but the CLTB-36 peptide did not produce AB or CTL immune responses against p24 or gp160				
Pol	Pol (172–219 subtype B)		Vaccine	human	Gorse1999b
	Vaccine *Vector/Type:* canarypox prime with rgp120 boost *Strain:* LAI and SF2 *HIV component:* Env, Gag, Pro, Nef, Pro • The vaccine used was rec canarypox expressing HIV-1 env, gag, pol, nef and protease (vCP300) with or without administration of HIV-1 SF-2 rgp120 • In vitro inducible CTL activity against HIV-1 Env, Gag, Pol, and Nef antigens was observed in 79% (15 of 19) of vaccine recipients • The combination of vCP300 and vP1291 together resulted in an overall increase in CTL induction and detection sensitivity				
Pol	Pol (IIIB)		HIV-1 infection	human	Betts1999
	• This study demonstrated an inverse correlation between HIV Type I plasma viral load and CTL activity directed against HIV-1 Pol, and stronger combined effects of Pol- and Env-specific CTL, in long-term survivors (LTS) of HIV-1 infection				
Pol	Pol (BRU)		HIV-1 infection	human	Aladdin1999
	• In vitro measurements of CTL-activity by Cr release assay in bulk culture showed no correlation between CTL-activity (gp120, Gag, Pol and Nef) and disease progression as measured by viral load, CD4 and time to death				
Pol	RT (LAI)		HIV-1 infection	human	Buseyne1998b
	• In infants with positive CTL responses, most responses showed cross-clade reactivity with somewhat diminished recognition of epitopes from different subtypes				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Pol	RT		Vaccine	murine	Kim1997c
	Vaccine *Vector/Type:* DNA *HIV component:* Gag, Pol, Vif, Env *Adjuvant:* B7, IL-12				
	• A gag/pol, vif or gp160 DNA vaccine, when delivered in conjunction with the plasmid encoding the co-stimulatory molecules B7 and IL-12, gave a dramatic increase in both the cytotoxic and proliferative responses in mice				
	• When IL-12 was present, CTL response could be detected even without in vitro stimulation				
Pol	RT		HIV-1 infection	human	Trickett1998
	• Twelve HIV-1 infected patients were re-infused with their own lymphocytes, cryopreserved from an earlier time point in the infection				
	• Improvement in CD4+ and CD8+ T cells were seen in 7/12, and an increase in the CTL response to Pol was seen in one patient				
Pol	RT		HIV-1 infection	human	Froebel1997
	• Two HIV-1 infected children with contrasting disease courses were followed longitudinally – one died of AIDS, the other is a long-term non-progressor				
	• Reactivity against Gag, Pol, Env and Tat proteins was tested by PBMC bulk cultured cells reacting with protein expressed in vaccinia constructs in autologous EBV transformed B cells				
	• The child who progressed consistently had CTL against Pol and Tat				
	• The long-term non-progressing child had no detectable CTL, but was heterozygous for a mutation in the CCR5 receptor and for HLA-B49, which has been shown to be associated with slower progression				
Pol	Pol (IIIB)		HIV-1 infection	human	Betts1997
	• 6/8 individuals from Zambia infected with C clade virus had CTL that were able to make response to B clade HIV-1 IIIB vaccinia-expressed Gag, Pol and Env proteins				
	• A vigorous cross-clade response was not limited to a particular protein, and the level of recognition of different proteins varied among the six patients				
Pol	RT		HIV-1 infection	human	De Maria1997
	• CD3+ cells that also carry a natural killer cell receptor (NKR+) can exhibit down regulation of T cell function				
	• Anti-NKR IgM MAb masked this inhibitory function and increased HIV-1 specific CTL activity in phytohemagglutinin-activated PBMC cultured in the presence of IL-2 from 3/5 patients, and in one other case anti-NKR MAb brought HIV-1 specific CTL activity to detectable levels				
Pol	Pol (LAI, MN)		HIV-1 exposed seronegative	human	Goh1999
	• 13/37 exposed uninfected individuals with repeated high-risk sexual exposure had HIV-1 specific CTL against Env, Gag, Pol, or a combination of proteins – CTL activity was correlated with a CCR5 wildtype genotype				
	• In this group, the highest CTLp frequencies were directed at Gag, but the most common response was to Env and four individuals had responses to multiple HIV-1 proteins				
Pol	Pol (LAI)		Vaccine	human	Evans1999
	Vaccine *Vector/Type:* canarypox *HIV component:* gp120, gp41, Gag, Pro, Nef, RT				
	• A Canarypox vaccine expressing gp120, gp41, Gag, Protease, Nef and Pol CTL epitopes gave rise to CTL that could be detected in 61% of the volunteers – responses to Gag, Env, Nef and Pol were detected 3-6 months after the last vaccination				
Pol	Gag/Pol (MN)		Vaccine	chimpanzee	Kim1998
	Vaccine *Vector/Type:* DNA *HIV component:* Env, Gag, Pol *Adjuvant:* CD86, CD80				
	• The study explores the use of co-stimulatory molecules co-expressed with an HIV-1 immunogen in a DNA vaccine to enhance the immune response – co-expression of CD86, but not CD80, dramatically increased both HIV Env and Gag/Pol specific CTL and Th proliferative responses				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Pol	Pol (IIIB)		HIV-1 infection	human	Jin1998a
• CTL precursor frequencies were determined in HIV-1 infected pregnant women, and significantly higher CTLp frequencies to Pol and Nef were found in non-transmitting mothers than in transmitting mothers;					
Pol	Pol		HIV-1 infection	human	Young2001
• Addition of recombinant rec human IL12 (rhIL12) to cultures increased HIV-specific lysis of HIV-Gag, Pol and gp120 vaccinia expressed antigens (11/15 tested increased lysis by > 5%) if the culture was derived from HIV+ individuals who had CD4 cells/ul > 500 • 2/10 individuals with <200 CD4 cells/ul, and 3/10 individuals with 200-500 CD4cells/ul, had an increase of >5% upon treatment of the culture with rhIL12, so a few individuals in late stage disease had CD8 cells that maintained responsiveness to rhIL12					
Pol	RT (subtype A, B, D)		HIV-1 infection	human	Cao2000
• HIV-1 subtypes A and D dominate the Ugandan epidemic, and a vaccine trial using B clade antigen is underway – this study addresses relative levels of cross-reactive CTL responses in HIV infected Ugandans to A, D, and B clade recombinant vaccinia viruses expressing Gag, Env, Pol, RT or Nef from HIV-1 clades A, B, and D. • Proteins corresponding to the subtype of the infecting strains tended to trigger higher levels of CTL response measured by percent specific lysis, but there was extensive inter-subtype cross-reactivity with B clade proteins and the co-circulating subtype.					
Pol	Pol		HIV-1 infection	human	White2001
• HIV-specific CTL activity was detected in the female reproductive tract of only 1/3 HIV-infected women who underwent a hysterectomy, although CTL could be identified in the PBMC of all three women					
Pol	Pol (IIIB)		HIV-1 infection	human	Jin2000a
• The CTL precursor level (CTLp) was measured in long term non-progressors (LTNP) with low viral load using limiting dilution analysis and measuring CTL against Env Gag and Pol expressed in vaccinia in autologous targets • LTNPs have high memory CTL numbers and low viral load					
Pol	Pol		HIV-1 exposed seronegative	human	Rowland-Jones2001
• This is a review that summarizes observations about HIV-specific CTL found in the HIV-1 exposed persistently seronegative (HEPS) population • The CTL responses assayed by ELISPOT and by CTL precursor frequencies by limiting dilution analysis indicate that CTL in HEPS individuals tend to be of a lower magnitude than in chronic HIV-1 infections – the responses in HEPS cases are below the level of detection by tetramer assays • CD8+ CTL responses tend to be detectable in HEPS subjects only if they are recently exposed, and the response diminishes if exposure is reduced – it is not clear if there is a stable memory population in HEPS cases • CD8+ CTL responses in the HEPS population are associated with HIV-1 specific CD4+ T cell responses, assayed by proliferation assays, IL-2 secretion, and ELISPOT, and the authors consider the possibility that HIV-1-specific T-help responses improve the "quality" of the CD8+ response in HEPS individuals relative to HIV-1 infected individuals, who tend to have a poor HIV-1-specific T-help response • HIV-1 specific CD8+ CTL responses in HIV-1 infected individuals show reduced levels of perforin, and the T cells may not mature properly, and although similar studies have not been conducted in HEPS individuals this is considered as a possible difference in the CTL immune response in HEPS and HIV-1 infected people					
Pol			HIV-1 exposed seronegative	human	De Maria1994, Kuhn2002
• 6/24 HIV uninfected infants (ages 15-50 months) born to HIV+ mothers had HIV-1 specific CTL responses to vaccinia-expressed Nef, Gag/Pol, Env. • Reviewed in [Kuhn2002].					

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Pol			HIV-1 infection	human	Kuhn2002, Wasik1999
• In HIV-infected infants HIV-specific, CTL responses were not detectable in icord blood or in PBMC collected shortly after birth and were absent or remained very low in 3 infants with a rapidly progressive disease. For those who progressed more slowly, the HIV-specific CTL activity varied. • The two infants with high levels of Env peptide-stimulated IL-2 responses had the highest CTLp frequencies. • Stronger responses were detected after initiation of the antiretroviral therapy. • Two babies that were not infected though born to HIV+ mothers had detectable though low HIV-specific CTLp responses to Env (1/2), Pol (2/2), Gag (1/2) cord blood and transiently in PBMC after birth. • Reviewed in [Kuhn2002].					
Pol			HIV-1 infection	human	Aldhous1994, Kuhn2002
• Six of nine HIV vertically infected infants had HIV-1 specific CTL responses to vaccinia expressed Tat (4/6), Pol (6/6), Env (1/6), or Gag (1/6), but not all responses were detected at all time points. • Two of eleven babies that were not infected though born to HIV+ mothers had detectable responses Tat (1/2), Pol (2/2), Gag (1/2). • Reviewed in [Kuhn2002].					
Pol			HIV-1 infection	human	Yusim2002
• Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17. • In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed, however, epitopes were not found that span the invariant, most highly conserved regions of RT and Protease. This might be due to the virus evolving conserved features that disallow the CTL responses in these most conserved regions, as functional constraints for enzyme function would not tolerate change and normal capacity for immune escape by rapid evolution is lost in these domains.					
Pol			HIV-1 infection	human	Loemba2002
• Therapeutic RT inhibitors were used to select in vitro for resistance mutations in subtype C viruses. Many of the resistance mutations were located within analogs to CTL epitopes that had been defined for the B subtype,					
Pol	(IIIB)		HIV-1 infection	human	Ortiz2002
• Subjects treated with HAART early in HIV-infection showed a correlation between the number of viremic episodes and the total as well as the Pol-specific CD8 T-cell activity as measured by Elispot SFC per million PBMC summed across Pol, Env, Nef and Gag. The subjects treated early after infection had higher levels of CD8+ T-cell activity (N = 31) than those treated later (N = 23), and a greater capacity to enhance CD8+ T-cell responses to viremic episodes.					
Pol	(MN)		HIV-1 infection	human	Edwards2002
• 96% (26/27) chronically infected HIV-1 infected patients elicited gamma-IFN CD8+ T-cell responses against Gag • Nef and/or Pol CTL responses were detected in 86% of the subjects • The magnitude and breadth of Gag and p24 T-cell responses correlated with absolute CD4 counts, and inversely correlated with viral load • Pol and Int CTL responses correlated positively with absolute CD4+ T-cell count • Nef and Env responses did not correlate with either CD4 counts or viral load					
Pol			HIV-1 infection	human	Larsson2002b
• Autologous mature dendritic cells with rec vaccinia expressing Gag, Pol, Nef and Env could amplify CD8+ T-cell Elispot responses 4-38 fold in five HIV+ patients on successful HAART treatment, relative to autologous monocytes. Some weak responses could only be detected using mature dendritic cells as APCs, and this approach could be useful for detection of low frequency memory cells.					

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Pol	(IIIB)		HIV-1 infection	human	Trickett2002
• Conditions were optimized for ex-vivo expansion of CD8+ and CD4+ T-cells with the goal of functional T-cell production for autologous immunotherapy. 10,000-fold expansions were obtained in 14 days with optimized concentrations of IL-2, anti-CD3 and anti-CD28 coated microspheres, and decreasing amounts of serum over the first 8 days.					
Pol	(IIIB)		HIV-1 and HCV co-infection	human	Lauer2002
• HIV-1 and HCV immune responses were studied in 22 individuals who were co-infected with HIV-1 and hepatitis C virus (HCV). IFNgamma production was measured in an Elispot assay of CD8+ T-cells using targets expressing either Gag, RT, Env and Nef in a vaccinia construct, or one of seven HCV proteins.					
• All 22 patients targeted at least one protein. 20/22 patients recognized RT, 17/22 patients recognized Gag, 13/22 subjects recognized Env and 11/22 patients recognized Nef. Robust CTL activity was independent of disease progression or viral load.					
• Despite high HCV viral loads, very few HCV CD8+ T-cell Elispot responses were detected. In a control HCV infected person who did not have HIV-1, strong anti-HCV responses were mounted.					
• HIV-specific CD4 proliferative responses were detected in 9/17 coinfected patients, but no HCV responses were detected.					
Pol			HIV-1 infection	human	Scott2001
• CTL responses before and after initiation of ART were studied in 13 HIV-1 vertically infected infants <6 months of age, and 4 that were >6 months of age.					
• Before ART 2/13 infants <6 months of age showed IFNgamma Elispot CD8+ T-cell responses, one to Nef and one to Env and Nef, and these responses became undetectable after successful therapy– 3 infants were coinfected with CMV and all 3 had CMV-specific CD8+ T-cell responses.					
• One older infant, at 23 months, had CTL responses against all for proteins tested, Gag, Pol, Nef and Env, and had the lowest plasma viremia of the study group. 3/4 infants older than 6 months of age responded to either Nef or Pol.					
• Administration of ART over 48 weeks broadened the HIV-1-specific CTL response in 2/4 of the older children that were incomplete responders.					
Pol	(IIIB, MN)		HIV-1 infection	human	Larsson2002a
• Dendritic cells acquire and present HIV-1 antigens derived from dead, apoptotic cells or from non-infectious, fusion-competent HIV-1 virions, and these DC cells could stimulate CD4+ and CD8+ T-cells resulting in IFNgamma production in an Elispot assay. Both HLA Class I and class II molecules were used for presentation. This may be an important aspect of the initial immune response to HIV-1 infection of CD4+ cells in the mucosal subepithelia.					
Pol	(IIIB)		HIV-1 infection	human	Ortiz2001
• Immune responses in eight chronically HIV-1 infected patients undergoing HAART therapy structured treatment interruptions (STI) were studied. STI boosted HIV-1 specific CTL responses and elevated CTL responses were maintained up to 22 weeks after the last treatment interruption, but viral load rebound to pretreatment levels and CD4 T-cell count decline was observed. CD8 responses in PBMC were measured by cytokine flow cytometry with gp160, Gag p55, RT-Pol and Nef expressed in vaccinia.					
Pol	Pol		HIV-1 infection	human (A*0201 and Cw*08)	Shacklett2000
• HIV-1 specific, MHC class I-restricted CTL killing was detected in duodenal and rectal gut associated lymphoid tissue (GALT) sites from three infected individuals – the distribution of class I restricted CTL was different in the peripheral blood samples and GALT samples					
Pol			computer prediction	(A*0201, B*3501)	Schönbach2002
• Computational methods (artificial neural networks, hidden Markov models, binding matrices based on HLA association rates) were used to identify HLA-A*0201 and HLA-B*3501 HIV T-cell epitope candidates from 533 Gag, Env and Pol sequences of which 374 were derived from HIV-1, 97 were derived from HIV-2 and 62 from SIV. Comparisons to known epitopes and between clades were made.					

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Pol	RT (IIIB)		HIV-1 infection	human (A2)	Moore2002b
	• HIV polymorphisms in the RT protein were examined relation to HLA alleles found in a population of 473 participants in the Western Australian HIV Cohort Study. 64 significant associations between polymorphisms at particular positions and HLA alleles were detected, for HLA-B7, -B12, -B35 and -B15. Fifteen of these were in positions with known epitopes, 4 in anchor residues, 11 in other positions. Six additional polymorphic sites associated with particular HLA molecules flanked known epitopes and may relate to processing. • 25 negative associations were also found between polymorphism and HLA alleles. The authors propose this is due to escape mutations in epitopes presented by common HLA types dominating in the population, and give examples of five amino acids which are in the consensus and tend to be stable in those with the most common HLA allele, HLA-A2.				
Pol	Pol		HIV-1 infection	human (B*35)	Jin2002
	• Patients with HLA-B*35 variants B*3502, B*3503, B*3504, and B*5301 tend to proceed to AIDS more quickly than those with B*3501. • Of 32 patients with HLA-B*35 alleles CD8+ CTL responses were quantified using an intracellular cytokine staining assay – 75% had responses to Pol, 69% to Gag, 50% to Nef, and 41% to Env. • The overall magnitude of CTL responses did not differ between those bearing B*3501 and the others. A higher percentage of Gag responses was observed in those that had lower RNA levels that carried B*3501, and there was a negative association with viral load and CTL activity. The data is consistent with higher levels of CTL responses contributing to protection in B*3501 individuals, but not in B*3502, B*3503, B*3504, and B*5301 individuals.				
Pol	Pol		Vaccine	murine (H-2^d)	Huang2001
	Vaccine *Vector/Type:* DNA *Strain:* gag HxB2, pol NL43 *HIV component:* Gag, Pol • Mice were immunized with four humanized DNA constructs: GagPol, that would form a pseudoparticle carrying Gag and Pol, Gag, Pol or a GagPol fusion construct • The GagPol pseudoparticle, Gag and GagPol fusion construct all elicited strong anti-Gag CTL, but only the GagPol fusion construct elicited strong anti -Pol CTL				

II-B-13 Vif CTL Epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Vif (17–26)		RIRTWKSLVK	HIV-1 infection	human	Yusim2002
	• Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17. • While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins. • In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed. • What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.			
Vif (17–26)	Vif (17–26 SF2)	RIRTWKSLVK	HIV-1 infection	human (A*0301)	Altfeld2001a
	• Epitope name: RK10 • CTL responses against HIV-1 Vpr, Vpu, and Vif were analyzed in multiple HIV-1-infected individuals • 10/29 (35%) individuals tested responded to Vif • This epitope was recognized by 3/15 individuals expressing A*0301 allele • HIV+ individual AC-06 was tested for reactive overlapping peptides spanning all HIV-1 proteins in an ELISPOT and was found to react with 12 peptides from 7 proteins, suggesting that the breadth of CTL responses are underestimated if accessory proteins are not included in the study • Overlapping Vif peptides QVDRMRIRTWKSLVK and RIRTWKSLVKHHMYI both reacted with T-cells from AC-06 and contained epitope RIRTWKSLVK				
Vif (17–26)	Vif (17–26)	RIRTWKSLVK	HIV-1 infection	human (A*0301)	Addo2002b
	• CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot. • 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides. • All known optimally defined epitopes were summarized for the five proteins.				
Vif (17–26)		RIRTWKSLVK	HIV-1 infection	human (A03)	Sabbaj2002b
	• Epitope name: Vif-RK10 • Among HIV+ individuals who carried HLA A03, 3/21 (14%) recognized this epitope				
Vif (17–26)	(LAI)	RIRTWKSLVK		(A3)	Altfeld2000a, Brander2001
Vif (17–26)	Vif (17–26)	RIRTWKSLVK	HIV-1 infection	human (A3)	Yu2002a
	• Epitope name: A3-RK10 • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• 0/14 HLA-A3 positive individuals had detectable A3-restricted responses to this epitope during acute infection, but only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 1/7 individuals had detectable responses to this epitope after STI.				
Vif (27–41)	Vif	HHMYISKKAKGWGWFYR	HIV-1 infection	human	Addo2002b
	• CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot – 33% (23/70) targeted one or more Vif peptides, and this peptide was the most frequently recognized epitope in Vif (25%). • The regulatory proteins Rev and Tat combined contributed to 3%, and the accessory proteins Vif, Vpr and Vpu to 7%, of the total magnitude of HIV-1 specific CTL responses in a subset of 22 HIV-1 infected individuals in whom all HIV-1 proteins were studied.				
Vif (28–36)	Vif (28–36)	HMYISKKAK	HIV-1 infection	human (A*0301)	Addo2002b
	• CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot. • 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides. • All known optimally defined epitopes were summarized for the five proteins.				
Vif (28–36)	Vif (28–36)	HMYISKKAK	HIV-1 infection	human (A3)	Yu2002a
	• Epitope name: A3-HK9 • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 0/14 HLA-A3 positive individuals had detectable A3-restricted responses to this epitope during acute infection, but only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 2/7 individuals had detectable responses to this epitope after STI.				
Vif (31–39)		ISKKAKGWF	HIV-1 infection	human	Yusim2002
	• Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17. • While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins. • In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed. • What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.				
Vif (31–39)	Vif (31–39 SF2)	ISKKAKGWF	HIV-1 infection	human (B*5701)	Altfeld2001a
	• CTL responses against HIV-1 Vpr, Vpu, and Vif were analyzed in multiple HIV-1-infected individuals • 10/29 (35%) individuals tested responded to Vif • This epitope was recognized by 2/6 individuals expressing B*5701 allele				
Vif (31–39)	Vif (31–39)	ISKKAKGWF	HIV-1 infection	human (B*5701)	Addo2002b
	• CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot. • 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• All known optimally defined epitopes were summarized for the five proteins.				
Vif (48–57)		HPRVSSEVHI	HIV-1 infection	human	Yusim2002
	• Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17. • While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins. • In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed. • What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.				
Vif (48–57)	Vif (48–57 SF2)	HPRVSSEVHI	HIV-1 infection	human (B*0702)	Altfeld2001a
	• Epitope name: HI10 • CTL responses against HIV-1 Vpr, Vpu, and Vif were analyzed in multiple HIV-1-infected individuals • 10/29 (35%) individuals tested responded to Vif • This epitope was recognized by 3/8 individuals expressing B*0702 allele • HIV+ individual AC-06 was tested for reactive overlapping peptides spanning all HIV-1 proteins in an ELISPOT and was found to react with 12 peptides from 7 proteins, suggesting that the breadth of CTL responses are underestimated if accessory proteins are not included in the study • Overlapping Vif peptides HHYESTHPRVSSEVH and THPRVSSEVHIPLG both reacted with T-cells from AC-06 and contained epitope HPRVSSEVHI				
Vif (48–57)	Vif (48–57)	HPRVSSVHI	HIV-1 infection	human (B*0702)	Addo2002b
	• CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot. • 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides. • All known optimally defined epitopes were summarized for the five proteins.				
Vif (48–57)	Vif (48–57)	HPRVSSEVHI	HIV-1 infection	human (B7)	Yu2002a
	• Epitope name: B7-HI10 • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 0/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. 2/4 individuals had detectable responses to this epitope after STI.				
Vif (61–80)	Vif (61–80)	EARLVIKTYWGLOTGERDWH	HIV-1 infection	human	Novitsky2002
	• HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Vif (71–90)	Vif (71–90)	GLQTGERDWHLGHGVSIEWR	HIV-1 infection	human	Novitsky2002
	• HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
Vif (102–111)		LADQLIHLHY	HIV-1 infection	human	Yusim2002
	• Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17. • While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins. • In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed. • What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.				
Vif (102–111)	Vif (102–111 SF2)	LADQLIHLHY	HIV-1 infection	human (B*1801)	Altfeld2001a
	• CTL responses against HIV-1 Vpr, Vpu, and Vif were analyzed in multiple HIV-1-infected individuals • 10/29 (35%) individuals tested responded to Vif • This epitope was recognized by 2/5 individuals expressing B*1801 allele				
Vif (102–111)	Vif (102–111)	LADQLIHLHY	HIV-1 infection	human (B*1801)	Addo2002b
	• CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot. • 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides. • All known optimally defined epitopes were summarized for the five proteins.				
Vif (158–168)	Vif (158–168)	KTKPPLPSVKK	HIV-1 infection	human (A*0301)	Addo2002b
	• CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot. • 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides. • All known optimally defined epitopes were summarized for the five proteins.				
Vif (158–168)	Vif (158–168)	KTKPPLPSVKK	HIV-1 infection	human (A3)	Yu2002a
	• Epitope name: A3-KK11 • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 0/14 HLA-A3 positive individuals had detectable A3-restricted responses to this epitope during acute infection, but only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 2/7 individuals had detectable responses to this epitope after STI.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Vif (160–169)	Vif	KPPLPSVKKL		human (B7)	De Groot2001
	• The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes • A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes could stimulate IFNγ production in an ELISPOT assay • KPPLPSVKKL was newly identified as an HLA-B7 epitope in this study				
Vif	Vif		Vaccine	murine	Kim1997c
	Vaccine *Vector/Type:* DNA *HIV component:* Gag, Pol, Vif, Env *Adjuvant:* B7, IL-12 • A gag/pol, vif or env DNA vaccine, when delivered in conjunction with the plasmid encoding the co-stimulatory molecules B7 and IL-12, gave a dramatic increase in both the cytotoxic and proliferative responses in mice • When IL-12 was present, CTL response could be detected even without in vitro stimulation				
Vif	Vif		Vaccine	murine (H-2^d)	Ayyavoo2000
	Vaccine *Vector/Type:* DNA *HIV component:* Vif, Vpu, Nef • Splenocytes from BALB/c mice immunized with pVVN-P DNA were incubated with Vif, Vpu or Nef antigens for 3 days and assayed for IL-4 and IFN-gamma levels • Antigen stimulation increased IFN-gamma production in pVVN-P immunized mice, indicating a Th1 response • IL-4 production was not significantly changed after antigen stimulation compared to control levels • Cross-clade CTL activity was also observed: A, B clade, CRF01(AE) clade antigens could serve as targets for the B clade immunization-stimulated CTL – an HIV-1 AC recombinant, however, did not stimulate a CTL response, but was expressed at lower levels on the target cell				
Vif	Vif		Vaccine	murine (H-2^d)	Ayyavoo2000
	Vaccine *Vector/Type:* DNA *HIV component:* Vif, Vpu, Nef • Splenocytes from BALB/c mice immunized with pVVN-P DNA were incubated with Vif, Vpu or Nef antigens for 3 days and assayed for IL-4 and IFN-gamma levels • Antigen stimulation increased IFN-gamma production in pVVN-P immunized mice, indicating a Th1 response • IL-4 production was not significantly changed after antigen stimulation compared to control levels • Cross-clade CTL activity was also observed: A, B clade, CRF01(AE) clade antigens could serve as targets for the B clade immunization-stimulated CTL – an HIV-1 AC recombinant, however, did not stimulate a CTL response, but was expressed at lower levels on the target cell				

II-B-14 Vpr CTL Epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Vpr (12–20)		REPHNEWTL	HIV-1 infection	human	Yusim2002
	• Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17. • While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins. • In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed. • What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.			
Vpr (12–20)	Vpr (12–20 SF2)	REPHNEWTL	HIV-1 infection	human (B*4002)	Altfeld2001a
	• CTL responses against HIV-1 Vpr, Vpu, and Vif were analyzed in multiple HIV-1-infected individuals • Individuals with long-term nonprogressive and treated chronic HIV-1 infection targeted Vpr more frequently than individuals with treated acute infection • Only one B*4002+ individual was tested, and had a CTL response against REPHNEWTL • Vpr is a frequent target of HIV-1 specific CD8+ T-cells – a response was detected in 45% of individuals tested and Vpr and p17 were the most preferentially targeted proteins per unit length by CD8+ T-cells				
Vpr (12–20)	Vpr (12–20)	REPHNEWTL	HIV-1 infection	human (B*4002)	Addo2002b
	• CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot. • 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides. • All known optimally defined epitopes were summarized for the five proteins.				
Vpr (30–38)		AVRHFRPIW	HIV-1 infection	human	Yusim2002
	• Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17. • While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins. • In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed. • What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.			
Vpr (30–38)	Vpr (29–38 SF2)	AVRHFPRIW	HIV-1 infection	human (B*5701)	Altfeld2001a
	• CTL responses against HIV-1 Vpr, Vpu, and Vif were analyzed in multiple HIV-1-infected individuals • This epitope was recognized by 4/6 individuals expressing B*5701 allele				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Individuals with long-term nonprogressive and treated chronic HIV-1 infection targeted Vpr more frequently than individuals with treated acute infection • Vpr is a frequent target of HIV-1 specific CD8+ T-cells – a response was detected in 45% of individuals tested and Vpr and p17 were the most preferentially targeted proteins per unit length by CD8+ T-cells				
Vpr (30–38)	Vpr (29–38)	AVRHFPRIW	HIV-1 infection	human (B*5701)	Addo2002b
	• CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot. • 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides. • All known optimally defined epitopes were summarized for the five proteins.				
Vpr (30–38)		AVRHFPRIW	HIV-1 infection	human (B57)	Sabbaj2002b
	• Epitope name: Vpr-AW9 • Among HIV+ individuals who carried HLA B57, 1/7 (14%) recognized this epitope				
Vpr (31–50)	Vpr (31–50)	VRHFPRPWLHSLGQYIYETY	HIV-1 infection	human	Novitsky2002
	• HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 8 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
Vpr (34–42)		FPRIWLHGL	HIV-1 infection	human	Yusim2002
	• Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17. • While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins. • In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed. • What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.				
Vpr (34–42)	Vpr (34–42 SF2)	FPRIWLHGL	HIV-1 infection	human (B*0702)	Altfeld2001a
	• Epitope name: FL9 • CTL responses against HIV-1 Vpr, Vpu, and Vif were analyzed in multiple HIV-1-infected individuals • This epitope was recognized by 2/2 individuals expressing B*8101 allele and 4/8 individuals expressing B*0702 allele • Individuals with long-term nonprogressive and treated chronic HIV-1 infection targeted Vpr more frequently than individuals with treated acute infection • Vpr is a frequent target of HIV-1 specific CD8+ T-cells – a response was detected in 45% of individuals tested and Vpr and p17 were the most preferentially targeted proteins per unit length by CD8+ T-cells • HIV+ individual AC-06 was tested for reactive overlapping peptides spanning all HIV-1 proteins in an ELISPOT and was found to react with 12 peptides from 7 proteins, suggesting that the breadth of CTL responses are underestimated if accessory proteins are not included in the study • FPRIWLHGL was the only epitope identified in Vpr for AC-06				
Vpr (34–42)	Vpr (34–42)	FPRIWLHGL	HIV-1 infection	human (B*0702)	Addo2002b
	• CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides. • All known optimally defined epitopes were summarized for the five proteins.				
Vpr (34–42)	Vpr (34–42 SF2)	FPRIWLHGL	HIV-1 infection	human (B*8101)	Altfeld2001a
	• Epitope name: FL9 • CTL responses against HIV-1 Vpr, Vpu, and Vif were analyzed in multiple HIV-1-infected individuals • This epitope was recognized by 2/2 individuals expressing B*8101 allele and 4/8 individuals expressing B*0702 allele • Individuals with long-term nonprogressive and treated chronic HIV-1 infection targeted Vpr more frequently than individuals with treated acute infection • Vpr is a frequent target of HIV-1 specific CD8+ T-cells – a response was detected in 45% of individuals tested and Vpr and p17 were the most preferentially targeted proteins per unit length by CD8+ T-cells				
Vpr (34–42)	Vpr (34–42)	FPRIWLHGL	HIV-1 infection	human (B*8101)	Addo2002b
	• CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot. • 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides. • All known optimally defined epitopes were summarized for the five proteins.				
Vpr (34–42)	Vpr (34–42)	FPRIWLHGL	HIV-1 infection	human (B7)	Yu2002a
	• Epitope name: B7-FL9 • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 1/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. 2/4 individuals had detectable responses to this epitope after STI.				
Vpr (55–70)	Vpr	AGVEAIIRILQQLLFI	HIV-1 infection	human	Addo2002b
	• CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot – 40% (28/70) targeted one or more Vpr peptides, and this peptide was the most frequently recognized epitope in Vpr (41%). • The regulatory proteins Rev and Tat combined contributed to 3%, and the accessory proteins Vif, Vpr and Vpu to 7%, of the total magnitude of HIV-1 specific CTL responses in a subset of 22 HIV-1 infected individuals in whom all HIV-1 proteins were studied.				
Vpr (59–67)		AIIRILQQL	HIV-1 infection	human	Yusim2002
	• Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17. • While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins. • In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed. • What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Vpr (59–67)	Vpr (58–66 LAI)	AIIRILQQL		human (A*0201)	Altfeld2001c, Brander2001
	• C. Brander notes this is an A*0201 epitope				
Vpr (59–67)	Vpr (58–66 SF2)	AIIRILQQL	HIV-1 infection	human (A*0201)	Altfeld2001a
	• Epitope name: AL9 • CTL responses against HIV-1 Vpr, Vpu, and Vif were analyzed in multiple HIV-1-infected individuals • This epitope was recognized by 8/24 individuals expressing A*0201 allele • Epitope is located within a highly conserved alpha helix in Vpr • Individuals with long-term nonprogressive and treated chronic HIV-1 infection targeted Vpr more frequently than individuals with treated acute infection • Vpr is a frequent target of HIV-1 specific CD8+ T-cells – a response was detected in 45% of individuals tested and Vpr and p17 were the most preferentially targeted proteins per unit length by CD8+ T-cells • The A2 eptiopes Vpr AIIRLLQQL and p17 SLYNTVATL do not account for the dominance of Vpr and p17, the result holds even when HLA-A2+ individuals are excluded				
Vpr (59–67)	Vpr (59–)	AIIRILQQL	HIV-1 infection	human (A*0201)	Altfeld2001c
	• Epitope name: Vpr-59 • HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested • Three additional previously described HLA-A2 epitopes were added to the set of 20, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acute infected individuals recognized at least 1 (median of 1 and maximum of 2) • AIIRILQQL binds to four HLA-A2 supertype alleles: A*0203, A*0201, A*0206 and A*6802 (highest affinity), but not A*0202 • 5/22 individuals with chronic HIV-1 infection recognized this epitope, but with low magnitude responses in ELISPOT • 2/12 HLA-A2 patients with acute HIV-1 infection responded strongly to this peptide, but during chronic infection SL9 and Gag-386 tended to be immunodominant while Vpr-59 was weak and sub-dominant • One of the the acutely infected individuals, AC13, was HLA A*0201/68 B44/14 and also had a strong acute response to gp41 epitope SV10 SLLNATDIAV • This peptide was shown to be properly processed and presented in TAP-competent B-cell lines in vitro				
Vpr (59–67)	Vpr (58–66)	AIIRILQQL	HIV-1 infection	human (A*0201)	Addo2002b
	• CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot. • 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides. • All known optimally defined epitopes were summarized for the five proteins.				
Vpr (59–67)		AIIRILQQL	HIV-1 infection	human (A02)	Sabbaj2002b
	• Epitope name: Vpr-AL9 • Among HIV+ individuals who carried HLA A02, 4/35 (11%) recognized this epitope				
Vpr (59–67)	Vpr (59–)	AIIRILQQL	HIV-1 infection	human (A2)	Goulder2001a
	• Epitope name: AL9 • Data from patient AC13 suggest a role for this epitope in initial control of viremia in acute infection, as it is one of several subdominant CTL epitopes recognized during the initial decline in viremia • A CTL response to SL9, SLYNTVATL, was not evident until 18 months post-presentation				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Vpr (59–67)	Vpr (59–67 SF2)	AIIRILQQL	HIV-1 infection	human (A2)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-A2+ individuals that had a CTL response to this epitope broken down by group: 1/10 group 1, 0/6 group 2, and 0/4 group 3			
Vpr (59–67)	Vpr (59–67)	AIIRILQQL	HIV-1 infection	human (A2 supertype)	Propato2001
	• Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus • This epitope can bind four of the five HLA-A2 supertypes alleles (A*0201, A*020 2, A*0203, A*0206 and A*6802)			
Vpr (62–70)	Vpr (62–)	RILQQLLFI	HIV-1 infection	human (A*0201)	Altfeld2001c
	• Epitope name: Vpr-62 • HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested • Three additional previously described HLA-A2 epitopes were added to the set of 20, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acute infected individuals recognized at least 1 (median of 1 and maximum of 2) • This epitope binds to three HLA-A2 supertype alleles: A*0202, A*6802 (strongest affinity) and A*0203 • 3/22 chronically infected patients had a weak ELISPOT response to this epitope • 0/12 HLA-A2 patients with acute HIV-1 infection responded to this peptide			
Vpr (62–70)	Vpr (62–70)	RILQQLLFI	HIV-1 infection	human (A*0201)	Addo2002b
	• CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot. • 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides. • All known optimally defined epitopes were summarized for the five proteins.			
Vpr (62–70)	Vpr (62–70)	RILQQLLFI	HIV-1 infection	human (A2 supertype)	Propato2001
	• Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus • This epitope can bind three of the five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802			
Vpr			Vaccine	murine	Muthumani2002
	Vaccine *Vector/Type:* adenovirus *HIV component:* Vpr, Nef, Gag/Pol				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Vpr can cause cells to go into G2 arrest, and it surpresses immune cell activation and inflammatory cytokine production, so co-immunization of BALB/c mice with recombinant adenovirus expressing Vpr and HIV-1 antigens Nef or Gag/Pol was tested to see if Vpr reduced the immune response to the other HIV antigens. • Vpr compromised CD8+ T-cell lytic responses and T-helper proliferative responses in mice co-immunized with Vpr and Nef or Gag/Pol. • In vitro, Vpr reduced T-cell cytokine production of IL-12 and TNFalpha, indicative of Vpr-mediated immune suppression.				

II-B-15 Tat CTL Epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Tat (2–11)		WPVDPRLEPW	HIV-1 infection	human	Yusim2002
	• Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17. • While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins. • In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed. • What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.			
Tat (2–11)		EPVDPRLEPW	HIV-1 infection	human (B*5301)	Sabbaj2002b
	• Epitope name: Tat-EW10 • Among HIV+ individuals who carried HLA B*5301, 3/15 (20%) recognized this epitope				
Tat (2–11)	(LAI)	EPVDPRLEPW		(B53)	Addo2001, Brander2001
Tat (2–11)	Tat (2–11 BRU)	EPVDPRLEPW	HIV-1 infection	human (B53)	Addo2001
	• Epitope name: Tat 1 • Rev and Tat are expressed early in the virus life cycle and thus may be important targets for CTL against HIV early in infection and for vaccines – therefore CTL responses against Tat and Rev were screened using overlapping peptides • 11/57 (19.3%) HIV-1+ individuals recognized at least 1 Tat peptide, and 21/57 (37%) responded to at least 1 Rev peptide • EPVDPRLEPW was recognized by four individuals, but only two were B53, thus this epitope can probably be presented by other HLA alleles				
Tat (2–11)	Tat (2–11)	EPVDPRLEPW	HIV-1 infection	human (B53)	Addo2002b
	• CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot. • 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides. • All known optimally defined epitopes were summarized for the five proteins.				
Tat (16–30)	Tat (16–30)	SQPKTACNKCYCKRC	HIV-1 infection	human	Novitsky2002
	• HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
Tat (17–26)		QPKTACTTCY	HIV-1 infection	human	Yusim2002
	• Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins. • In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed. • What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.				
Tat (17–26)	Tat (17–26)	QPKTACTTCY	HIV-1 infection	human (B35)	Addo2002b
	• CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot. • 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides. • All known optimally defined epitopes were summarized for the five proteins.				
Tat (36–50)	(subtype C)	VCFQTKGLGISYGRK		human	Novitsky2001
	• This study is provides a survey of CTL responses and full length HIV-1 genome sequences from a C subtype infected Botswanan cohort • 17 of 46 patient reacted with Tat immunodominant peptide VCFQTKGLGISYGRK • Most of the CTL responses occurred despite a mismatch between the autologous viral sequence and peptide – complete matches were seen only in 4 of 19 cases (21%) and the mismatched CTL tended not to respond to the autologous viral peptide indicative of immune escape				
Tat (36–50)	Tat (36–50)	VCFQTKGLGISYGRK	HIV-1 infection	human	Novitsky2002
	• HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 8 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
Tat (36–52)	Tat	VCFTTKALGISYGRKKR	HIV-1 infection	human	Addo2002b
	• CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot – 28% (19/70) targeted one or more Tat peptides, and this peptide was the most frequently recognized epitope in Tat (27%). • The regulatory proteins Rev and Tat combined contributed to 3%, and the accessory proteins Vif, Vpr and Vpu to 7%, of the total magnitude of HIV-1 specific CTL responses in a subset of 22 HIV-1 infected individuals in whom all HIV-1 proteins were studied.				
Tat (38–47)	(subtype C)	FQTKGLGISY		human (B*1503)	Novitsky2001
	• Epitope name: T38-FY10 • This study is provides a survey of CTL responses and full length HIV-1 genome sequences from a C subtype infected Botswanan cohort • 17 of 46 patient reacted with Tat immunodominant peptide VCFQTKGLGISYGRK • FQTKGLGISY was the optimal epitope in the peptide VCFQTKGLGISYGRK among B*1503+ individuals				
Tat (39–49)	Tat (38–48)	ITKGLGISYGR	HIV-1 infection	human (A*6801)	Oxenius2002a
	• Epitope name: Tat-4.8 • This epitope and HLA-A*6801 presenting molecule were rapidly defined using a modified Elispot assay. • The 11-mer is the optimal epitope but A*6801 epitopes tolerate length variation.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Tat (39–49)	Tat (38–48)	ITKGLGISYGR	HIV-1 infection	human (A68)	Addo2002b
	• CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot. • 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides. • All known optimally defined epitopes were summarized for the five proteins.				
Tat (40–49)		TKALGISYGR	HIV-1 infection	human	Yusim2002
	• Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17. • While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins. • In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed. • What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.				
Tat (49–57)	Tat (49–57)	RKKRRQRRR		murine	Kim1997a
	• The Tat peptide RKKRRQRRR when conjugated to a protein can cause that protein to be taken up by APCs and presented to CTL • The system was demonstrated by vaccinating mice with an OVA-Tat peptide conjugate and immunizing H-2 K^b mice • The CTL response to the H-2 K^b specific OVA peptide SIINFEKL was stimulated				
Tat (49–57)	Tat (49–57)	RKKRRQRRR	Vaccine	murine (H-2^d)	Billaut-Mulot2001
	Vaccine *Vector/Type:* DNA with DNA boost, DNA with recombinant protein boost *Strain:* LAI *HIV component:* Gag, Tat, Nef *Adjuvant:* IL18 • DNA vaccinated BALB/c mice primed and boosted with the multiepitopic vaccine with IL18 showed lymphoproliferative responses 7 weeks post immunization • Strong but non-lasting HIV-specific CTL responses were detected by a Cr-release assay and DNA prime/DNA boost was more effective than DNA prime protein boost • Immunization with either the multiepitopic DNA or with the mixed DNA vaccine induced HIV-1 specific Th1 cytokines (IL-2 and IFN-gamma) • Co-administration of IL18 increased T-cell responses but decreased anti-HIV antibody levels				
Tat (83–92)	Tat	GPKESKKKVE		human (B58)	De Groot2001
	• The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes • A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes could stimulate IFNγ production in an ELISPOT assay • GPKESKKKVE was newly identified as an HLA-B58 epitope in this study				
Tat	Tat		Vaccine	human	Calarota1999
	Vaccine *Vector/Type:* DNA *HIV component:* Nef, Rev Tat • 9/9 HIV-1+ subjects were given one of three DNA vaccinations for nef, rev or tat, and novel proliferative and CTL responses were generated • The nef DNA immunization induced the highest and most consistent CTLp activity, IFN-gamma production, and IL-6 and IgG responses				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Highly active antiretroviral treatment (HAART) did not induce new HIV-specific CTL responses but reduced viral load, while DNA vaccination induced new immune responses but did not reduce viral load – thus this is a potentially complementary and promising combination				
Tat	Tat		HIV-1 infection	human	Froebel1997
	• Two HIV-1 infected children with contrasting disease courses were followed longitudinally – one died of AIDS, the other is a long-term non-progressor • Reactivity against Gag, Pol, Env and Tat proteins was tested by PBMC bulk cultured cells reacting with protein expressed in vaccinia constructs in autologous EBV transformed B cells • The child who progressed consistently had CTL against Pol and Tat • The long-term non-progressing child had no detectable CTL, but was heterozygous for a mutation in the CCR5 receptor and for HLA-B49, which has been shown to be associated with slower progression				
Tat	Tat		HIV-1 infection, Vaccine	human	Calarota2001
	Vaccine *Vector/Type:* DNA *HIV component:* Nef, Rev, Tat *Adjuvant:* CpG motifs • This review discusses the cellular immune response, and comments on the stimulatory role of CpG motifs and how HIV-1 DNA vaccines can boost the CTL and Th proliferative responses in asymptomatic HIV+ individuals				
Tat	Tat		Vaccine	macaque	Cafaro2001
	Vaccine *Vector/Type:* DNA *Strain:* BH-10 *HIV component:* Tat *Adjuvant:* CpG, ISCOM • Macaques (macaca fascicularis) were immunized with HIV-1 Tat on an adenovirus major late promotor in a plasmid with 23 CpG sequences, 12 unmethylated • The vaccinated animals contained a primary infection challenge with SHIV89.6P, preventing CD4+ T-cell decline in the animals, suggesting Tat may be useful at blocking viral replication at its early stage				
Tat			HIV-1 infection	human	Aldhous1994, Kuhn2002
	• Six of nine HIV vertically infected infants had HIV-1 specific CTL responses to vaccinia expressed Tat (4/6), Pol (6/6), Env (1/6), or Gag (1/6), but not all responses were detected at all time points. • Two of eleven babies that were not infected though born to HIV+ mothers had detectable responses to Tat (1/2), Pol (2/2), Gag (1/2). • Reviewed in [Kuhn2002].				
Tat	Tat		HIV-1 infection, Vaccine	human	Gruters2002
	• This paper is a review that makes a case for using Tat and Rev as part of a vaccine strategy. • CTL against Tat and Rev were found preferentially in long term non-progressors. • Tat/Rev vaccinations of macaques provided protection or reduction in viremia, with high levels of CTL providing protection from challenge, lower levels of CTL having lower viremia, while Gag/Pol vaccinations with did not result in decreased viremia. • Early expression of Tat/Rev may in part explain the enhanced benefit of a CTL response directed at these proteins, and CTL escape is more prominent in these proteins.				
Tat	Tat		Vaccine	murine (H-2^d)	Xin2001
	Vaccine *Vector/Type:* adeno-associated virus (AAV) *HIV component:* Env, Tat, Rev *Adjuvant:* IL2 • An AAV vector expressing HIV-1 env, tat, and rev genes (AAV-HIV vector) was used to vaccinate BALB/c mice • A single injection stimulated and long lasting serum IgG, fecal IgA, and HIV-specific CTL • Boosting enhanced the humoral response, and IL2 enhanced T-cell immunity.				

II-B-16 Rev CTL Epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Rev (9–23)	Rev (9–23 HXB2)	DEELIRTVRLIKLLY	HIV-1 infection	human	Blazevic1995
	• Induces both Th and CTL activities, no HLA restriction analysis performed				
Rev (11–23)	Rev (14–23)	KAVRRLIKFLY	HIV-1 infection	human (B*5701)	Addo2002b
	• CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot. • 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides. • All known optimally defined epitopes were summarized for the five proteins.				
Rev (11–23)	Rev (14–23)	KAVRRLIKFLY	HIV-1 infection	human (B*5801)	Addo2002b
	• CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot. • 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides. • All known optimally defined epitopes were summarized for the five proteins.				
Rev (12–31)	Rev (11–30 SF2)	LLKAVRLIKFLYQSNPPPNF	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • Only one subject had CTL that could recognize vaccinia-expressed LAI Rev • This subject had a CTL response to this peptide, and was HLA-A2, A24, B13, B35				
Rev (14–23)		KAVRLIKFLY	HIV-1 infection	human	Yusim2002
	• Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17. • While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins. • In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed. • What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.				
Rev (14–23)	Rev (14–23 subtype B)	KAVRLIKFLY		human (B*5701)	Addo2001, Brander2001
	• C. Brander notes this is a B*5701 epitope				
Rev (14–23)	Rev (14–23 BRU)	KAVRIKLFLY	HIV-1 infection	human (B*5701)	Addo2001
	• Rev and Tat are expressed early in the virus life cycle and thus may be important targets for CTL against HIV early in infection and for vaccines – therefore CTL responses against Tat and Rev were screened using overlapping peptides • 11/57 (19.3%) HIV-1+ individuals recognized at least 1 Tat peptide, and 21/57 (37%) responded to at least 1 Rev peptide • This epitope was also recognized by another individual in whom it was restricted by HLA*B5801, an allele closely related to HLA*B5701, suggesting cross-presentation by the two HLA alleles				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Rev (14–23)	Rev (14–23 subtype B)	KAVRLIKFLY		human (B*5801)	Addo2001, Brander2001
	• C. Brander notes this is a B*5801 epitope				
Rev (14–23)	Rev (14–23 BRU)	KAVRIKLFLY	HIV-1 infection	human (B*5801)	Addo2001
	• Rev and Tat are expressed early in the virus life cycle and thus may be important targets for CTL against HIV early in infection and for vaccines – therefore CTL responses against Tat and Rev were screened using overlapping peptides • 11/57 (19.3%) HIV-1+ individuals recognized at least 1 Tat peptide, and 21/57 (37%) responded to at least 1 Rev peptide • This epitope was also recognized by another individual in whom it was restricted by HLA*B5701, an allele closely related to HLA*B5801, suggesting cross-presentation by the two HLA alleles				
Rev (25–39)	Rev (25–39 HXB2)	SNPPPNPEGTRQARR	HIV-1 infection	human	Blazevic1995
	• Induces both Th and CTL activities, no HLA restriction analysis performed				
Rev (33–48)	Rev (33–48 HXB2)	GTRQARRNRRRRWRER	HIV-1 infection	human	Blazevic1995
	• Induces both Th and CTL activities, no HLA restriction analysis performed				
Rev (41–56)	Rev (41–56 HXB2)	RRRRWRERQRQIHSIS	HIV-1 infection	human	Blazevic1995
	• Induces both Th and CTL activities				
Rev (55–63)	Rev (55–63 LAI)	ISERILSTY	HIV-1 infection	human (A1)	vanBaalen1997
	• Predicted to be an HLA-A1 epitope based on anchor residues 2S and 9Y • Both forms LSGWL(L or I)STY, with intact anchors, were found in an HLA-A1+ individual with Rev-responsive CTL • An HLA-A1 individual who did not make a Rev response had lost the C-term anchor, ISGWILS(T or N)S • 3/7 long-term non-progressors and 0/5 progressors were positive for HLA-B57 (associated with prolonged survival) • CTLp frequencies to Rev and Tat were inversely correlated with rapid progression to AIDS, but not Gag, RT or Nef				
Rev (55–63)	Rev (55–63)	ISERILSTY	HIV-1 infection, HIV-1 exposed seronegative	human (A1)	Kaul2001a
	• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers				
Rev (57–66)		ERILSTYLGR	HIV-1 infection	human	Yusim2002
	• Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17. • While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins. • In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed. • What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Rev (57–66)	Rev (57–66)	ERILSTYLGR	HIV-1 infection	human (A3)	Yu2002a
• Epitope name: A3-ER10 • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 0/14 HLA-A3 positive individuals had detectable A3-restricted responses to this epitope during acute infection, but only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 1/7 individuals had detectable responses to this epitope after STI.					
Rev (58–66)	Rev (58–66)	RILSTYLGR	HIV-1 infection	human (A*0301)	Addo2002b
• CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot. • 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides. • All known optimally defined epitopes were summarized for the five proteins.					
Rev (66–81)	Rev	RSAEPVPLQLPPLERL	HIV-1 infection	human	Addo2002b
• CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot – 36% (25/70) targeted one or more Rev peptides, and this peptide was the most frequently recognized epitope in Rev (32%). • The regulatory proteins Rev and Tat combined contributed to 3%, and the accessory proteins Vif, Vpr and Vpu to 7%, of the total magnitude of HIV-1 specific CTL responses in a subset of 22 HIV-1 infected individuals in whom all HIV-1 proteins were studied.					
Rev (67–75)		SAEPVPLQL	HIV-1 infection	human	Yusim2002
• Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17. • While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins. • In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed. • What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.					
Rev (67–75)	Rev (65–77 BH10, LAI)	SAEPVPLQL	HIV-1 infection	human	Maksiutov2002
• This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins. • This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is GRSAEPVPLQLPP) has similarity with transforming growth factor beta binding protein protein I, fragment ARSAEPEVATAPP. • This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is EPVPLQLPPL) also has similarity with the epidermal growth factor receptor substrate 15, fragment EPVPMSLPPA.					
Rev (67–75)	(LAI)	SAEPVPLQL		(B14)	Brander2001, vanBaalen2000

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Rev (67–75)	Rev	SAEPVPLQL	HIV-1 infection	human (B14)	Schutten2001
	• Molecularly cloned primary NSI macrophage tropic strain 2.1 and SI non-macrophage tropic strain 1.2 were isolated from study participant ACH320 and use to infect irradiated XID mice that had been reconstituted with human PBMC from B14+ seronegative donors – results indicate CTL may favor selective outgrowth of macrophage tropic strains • The CTL clone TCC108 specific for SAEPVPLQL, previously described by van Baalen 1997, and van Baalen 1998, was stimulated in vitro and given to the mice to apply specific CTL pressure • The macrophage-tropic HIV-1 strain #2.1 escaped CTL pressure more efficiently (7/14 animals) than its non-macrophage-tropic counterpart #1.2(SI) – the latter isolate was suppressed in 13/14 animals – macrophage may serve as a CTL sanctuary and reduced pressure on macrophage tropic HIV strains may allow additional replication to assist with acquisition of escape • Specific HIV-1 variants selectively induced by TCC108 were for strain 1.2: SEEPVPLQL, and for strain 2.1: SAEHVPLQL, SAESVPLQL, SVEPVPLQL, SLEPVPLQL, SAEPVPFQL, and SAEPVPFQL			
Rev (67–75)	Rev (67–75)	SAEPVPLQL	HIV-1 infection	human (B14)	vanBaalen2002
	• Tat, Rev and Nef are the first HIV proteins expressed upon acute infection of T-cells (< 6 hours), and RT is not expressed until after 24 hours. The B14-restricted Rev-SAEPVPLQL specific CD8 T-cell clone TCC108, and the B57-restricted RT-IVLPEKDSW specific CD8 T-cell clone TCL1C11 were co-incubated with CD4+ cultures innoculated with HIV-1 at low MOI. Co-incubation with the Rev-specific CTL resulted in two logs less HIV-1 production in ten days of culture. When the RT epitope was cloned into the Nef gene of the infecting strain, another early expressed protein, it proved as effective as the Rev epitope at inhibiting viral production. A mathematical model of CTL-target interactions suggest early proteins are important for vaccine design.				
Rev (67–75)	Rev (67–75)	SAEPVPLQL	HIV-1 infection	human (B14)	Addo2002b
	• CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot. • 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides. • All known optimally defined epitopes were summarized for the five proteins.				
Rev (67–75)	Rev (67–75 IIIB)	SAEPVPLQL	HIV-1 infection	human (B14, Cw8)	vanBaalen1998
	• The Rev-specific CTL response studied here was from an individual infected with HIV-1 for more than 12 years without developing symptoms – Rev and Tat are expressed early and CTL activity against these proteins has been correlated with long-term survival • The CTL clone TCC108 specific for this epitope was studied in vitro • CTLs added immediately after infection suppressed viral production, indicative of CTL interference with viral production prior to lysis – CTL-mediated lysis occurred after the onset of progeny viral release, but prior to peak viral production • Rapid selection of a E69K mutation, which abolished CTL, recognition was observed • The epitope was originally listed as B14, but Cw8 and B14 are in linkage disequilibrium, and in this case were not distinguished (Pers. Comm., Christian Brander, 1999)				
Rev (67–75)	(LAI)	SAEPVPLQL		human (Cw5)	Addo2001, Brander2001
Rev (67–75)	Rev (SF2)	SAEPVPLQL	HIV-1 infection	human (Cw5)	Goulder2001a
	• Epitope name: SL9 • Data from patient AC13 suggest a role for this epitope in initial control of viremia in acute infection, as it is one of several subdominant CTL epitopes recognized during the initial decline in viremia • A CTL response to SL9, SLYNTVATL, was not evident until 18 months post-presentation				
Rev (67–75)	Rev (67–75 SF2)	SAEPVPLQL	HIV-1 infection	human (Cw5)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-Cw5+ individuals that had a CTL response to this epitope broken down by group: 2/6 group 1, 0/1 group 2, and 0/2 group 3				
Rev (67–75)	Rev (67–75)	SAEPVPLQL	HIV-1 infection	human (Cw5/Cw8)	Addo2002b
	• CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot. • 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides. • All known optimally defined epitopes were summarized for the five proteins.				
Rev (67–75)	Rev (69–77 BRU)	SAEPVPLQL	HIV-1 infection	human (Cw8)	Addo2001
	• Epitope name: Rev SL9 • Rev and Tat are expressed early in the virus life cycle and thus may be important targets for CTL against HIV early in infection and for vaccines – therefore CTL responses against Tat and Rev were screened using overlapping peptides • 11/57 (19.3%) HIV-1+ individuals recognized at least 1 Tat peptide, and 21/57 (37%) responded to at least 1 Rev peptide • This epitope is the first HIV-specific CTL epitope resticted by HLA-Cw5 • This epitope was recognized by 2/5 individuals expressing HLA-Cw8 and by 5/11 individuals expressing Cw5 allele, which differs from Cw8 by 4 amino acids, suggesting promiscuous presentation of the epitope between those HLA molecules • Longitudinal data was available for 6 Rev-SL9 responders, who were treated during acute infection, and the response was stable 2 and 12 months after initiaion of HAART, measurements by ELISPOT and flow-based intracellular cytokine staining (ICS) were concordant – in two subjects the response was heightened by transient reexposure to antigen with treatment interruption at 12 to 14 months				
Rev (75–83)		LPPLERLTL	HIV-1 infection	human	Yusim2002
	• Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17. • While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins. • In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed. • What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.				
Rev	Rev		Vaccine	human	Calarota1999
	Vaccine *Vector/Type:* DNA *HIV component:* Nef, Rev Tat • 9/9 HIV-1+ subjects were given one of three DNA vaccinations for nef, rev or tat, and novel proliferative and CTL responses were generated • The nef DNA immunization induced the highest and most consistent CTLp activity, IFN-gamma production, and IL-6 and IgG responses • Highly active antiretroviral treatment (HAART) did not induce new HIV-specific CTL responses but reduced viral load, while DNA vaccination induced new immune responses but did not reduce viral load – thus this is a potentially complementary and promising combination				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Rev	(subtype C)			human	Novitsky2001
	• This study is provides a survey of CTL responses and full length HIV-1 genome sequences from a C subtype infected Botswanan cohort • Anti-Rev CTL responses were distributed throughout the protein and 27 of 47 subjects (57%) demonstrated HIV-1C Rev-specific ELISPOT CTL responses of more than 100 SFC/106 PBMC				
Rev	Rev		HIV-1 infection, Vaccine	human	Calarota2001
	Vaccine *Vector/Type:* DNA *HIV component:* Nef, Rev, Tat *Adjuvant:* CpG motifs • This review discusses the cellular immune response, and comments on the stimulatory role of CpG motifs and how HIV-1 DNA vaccines can boost the CTL and Th proliferative responses in asympotomatic HIV+ individuals				
Rev	Rev		HIV-1 infection, Vaccine	human	Gruters2002
	• This paper is a review that makes a case for using Tat and Rev as part of a vaccine strategy. • CTL against Tat and Rev were found preferentially in long term non-progressors. • Tat/Rev vaccinations of macaques provided protection or reduction in viremia, with high levels of CTL providing protection from challenge, lower levels of CTL having lower viremia, while Gag/Pol vaccinations with did not result in decreased viremia. • Early expression of Tat/Rev may in part explain the enhanced benefit of a CTL response directed at these proteins, and CTL escape is more prominent in these proteins.				
Rev	Rev		Vaccine	murine (H-2^d)	Ishii1997
	Vaccine *Vector/Type:* DNA with CMV promotor with cationic liposome *HIV component:* gp160, Rev • pCMV160/Rev is a DNA vaccine candidate carrying gp160 and Rev linked to a cytomegalovirus (CMV promotor) • pCMV160/Rev given in conjunction with a cationic liposome gave enhanced DTH, Ab and CTL responses				
Rev	Rev		Vaccine	murine (H-2^d)	Ihata1999
	Vaccine *Vector/Type:* DNA *HIV component:* rev *Adjuvant:* CD40 • pcRev DNA i.m. vaccination in BALB/c mice induced Th1, Th2 and IgG responses, and enhanced the CTL response to Rev, but did not induce mucosal IgA				
Rev	Rev		Vaccine	murine (H-2^d)	Xin2001
	Vaccine *Vector/Type:* adeno-associated virus (AAV) *HIV component:* Env, Tat, Rev *Adjuvant:* IL2 • An AAV vector expressing HIV-1 env, tat, and rev genes (AAV-HIV vector) was used to vaccinate BALB/c mice • A single injection stimulated and long lasting serum IgG, fecal IgA, and HIV-specific CTL • Boosting enhanced the humoral response, and IL2 enhanced T-cell immunity				

II-B-17 Vpu CTL Epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Vpu (4–13)	Vpu	LVILAIVALV		human (B7)	De Groot2001
	• The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes • A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes could stimulate IFNγ production in an ELISPOT assay • LVILAIVALV was newly identified as an HLA-B7 epitope in this study using ELISPOT, but could not be shown to bind to B7				
Vpu (25–40)	Vpu	IVFIEYRKLRQRKID	HIV-1 infection	human	Addo2002b
	• CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot – only 2% (2/70) targeted one or more Vpu peptides, including this peptide. • The regulatory proteins Rev and Tat combined contributed to 3%, and the accessory proteins Vif, Vpr and Vpu to 7%, of the total magnitude of HIV-1 specific CTL responses in a subset of 22 HIV-1 infected individuals in whom all HIV-1 proteins were studied.				
Vpu (29–37)	Vpu (29–37)	EYRLKILRQR	HIV-1 infection	human (A*3303)	Addo2002b
	• CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot. • 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides. • All known optimally defined epitopes were summarized for the five proteins.				
Vpu (29–37)	Vpu (29–37)	EYRLKILRQR	HIV-1 infection	human (A*3303)	Addo2002a
	• Detection of HIV CTL epitopes is rare in Vpu, and this is the first optimally defined Vpu epitope. • This CTL response was first detected in a long term non-progressor, and 3/6 HLA A*3303 positive individuals were found to have a CTL response to this epitope. • HLA A*3303 is common in West Africa and Asia.				
Vpu	Vpu		Vaccine	murine (H-2^d)	Ayyavoo2000
	Vaccine *Vector/Type:* DNA *HIV component:* Vif, Vpu, Nef • Splenocytes from BALB/c mice immunized with pVVN-P DNA were incubated with Vif, Vpu or Nef antigens for 3 days and assayed for IL-4 and IFN-gamma levels • Antigen stimulation increased IFN-gamma production in pVVN-P immunized mice, indicating a Th1 response • IL-4 production was not significantly changed after antigen stimulation compared to control levels • Cross-clade CTL activity was also observed: A, B clade, CRF01(AE) clade antigens could serve as targets for the B clade immunization-stimulated CTL – an HIV-1 AC recombinant, however, did not stimulate a CTL response, but was expressed at lower levels on the target cell				

II-B-18 gp160 CTL Epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (2–10)	gp160 (2–10 IIIB) • C. Brander notes this is a B*0801 epitope	RVKEKYQHL	HIV-1 infection	human (B*0801)	Brander2001
gp160 (2–10)	gp160 (2–10 IIIB) • HIV IIIB proteins were used to define the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB • Type-specific epitope, unique to the LAI and IIIB because of a deletion of three amino acids that are present in all other subtype B HIV-1s • RVKGIRKNYQHL, a variant found in JRCSF, was not recognized • This epitope is in the signal sequence of gp120	RVKEKYQHL	HIV-1 infection	human (B8)	Sipsas1997
gp160 (2–10)	gp120 (2–10) • B8-restricted CTL accounted for about 1/3 of the total CTL response in one individual	RVKEKYQHL	HIV-1 infection	human (B8)	Day2001
gp160 (6–12)	gp120 (6–15 CM243 subtype CRF01) • Epitope name: E6-15 • This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand • HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed • This epitope after a second stimulation *in vitro* gave a weak response in HEPS study subject 186 who was HLA A2/A11	TQMNWPNLWK	HIV-1 exposed seronegative	human (A11)	Sriwanthana2001
gp160 (6–12)	gp120 (6–15 CM243 subtype CRF01) • HLA-A11 CRF01 (called subtype E in Bond et al.) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive • 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 finding and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified • This is one of the new A11 epitopes identified through the streamlined EpiMatrix method, and 2/8 tested FSWs recognized it • This epitope was not conserved in other subtypes, and exact matches were rare	TQMNWPNLWK	HIV-1 infection	human (A11)	Bond2001
gp160 (30–49)	gp120 • Peptide 7035.1: Almost all CD8+ T cells are CD28+ at birth, and the proportion of CD28-CD8+ cells increases with age – this study examines the contribution of CD8+CD28- cells to CTL memory pools for CTL clones specific for two persistent human viruses, CMV and HIV – clones were found to be similarly distributed in the CD28 depleted cell population • HIV CTL responses to 3 Env and 2 Gag peptides were studied • The clonal composition of the TCR Vbeta responses was studied and was found to be highly focused, with one TCR beta-chain sequence tending to dominate the peptide-specific response – clones to this epitope were Vbeta6	AAEQLWVTVYYGVPVWKEAT	HIV-1 infection	human (A11)	Weekes1999b
gp160 (31–39)	gp120 (30–38 SF2) • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection	AENLWVTVY	HIV-1 infection	human (B44)	Altfeld2001b

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-B44+ individuals that had a CTL response to this epitope broken down by group: 1/8 group 1, 2/3 group 2, and 3/4 group 3				
gp160 (31–39)	gp120 (30–38)	AENLWVTVY	HIV-1 infection	human (B44)	Day2001
gp160 (31–39)	gp120	AENLWVTVY	HIV-1 infection	human (B44)	Cao2002
	• AC2 is a B44 restricted CTL clone that recognizes AENLWVTVY. • CTL could be activated by a fusion protein of an HIV protein and anthrax lethal factor (LFn-HIV) that promotes antigen presenting cell uptake of exogenous protein and allows processing through the MHC class I pathway. This strategy for CTL detection could allow antigen presentation without generation of cells by the standard methods of using live viral vectors carrying a protein, or by loading the cells with peptides and by-passing processing.				
gp160 (31–40)	gp160 (30–39 WEAU)	AENLWVTVYY	HIV-1 infection	human (B*4402)	Brander2001
	• C. Brander notes this is a B*4402 epitope				
gp160 (31–40)	gp160 (30–39 WEAU)	AENLWVTVYY	HIV-1 infection	human (B44)	Borrow1997, Borrow1998, Goulder1997a
	• Two CTL lines from the patient WEAU were studied – one had an optimal peptide of (A)AENLWVTVYY, and the other (A)AENLWVTVY, and both responded equally well with one or two N-term Alanines • Rapidly post-infection, a strong immunodominant response was observed against this epitope • The naturally occurring forms of the peptide found in WEAU were tested as targets for early WEAU CTLs – the form TENLWVTVY was as reactive as the wild type AENLWVTVY – but the forms AKNLWVTVY, AGNLWVTVY, AANLWVTVY did not serve as targets • The glutamic acid in the second position is a B44 anchor residue • [Goulder1997a] and [Borrow1998] are reviews of immune escape that summarizes this study in the context of CTL escape to fixation				
gp160 (31–55)	gp120 (32–56 LAI)	TEKLWVTVYYGVPVWKEAT-TTLFCA	Vaccine	human (B18)	Johnson1994a
	Vaccine *Vector/Type:* vaccinia *HIV component:* gp160 • HLA restricted CTL response to epitope in HIV-1 vaccinia-env vaccinees				
gp160 (31–55)	gp120 (32–56 LAI)	TEKLWVTVYYGVPVWKEAT-TTLFCA	Vaccine	human (B18)	Ferris1999, Hammond1995
	Vaccine *Vector/Type:* vaccinia *HIV component:* gp160 • This peptide can be processed for HLA-B18 presentation by both TAP-1/2 independent and dependent pathways				
gp160 (33–42)	gp120 (32–41 LAI)	KLWVTVYYGV	Vaccine	human (A2)	Dupuis1995
	Vaccine *Vector/Type:* recombinant protein *Strain:* MN *HIV component:* gp160 • CTL from HLA-A2 positive subject react with this peptide				
gp160 (33–42)	Env (32–41 subtype B)	KLWVTVYYGV	HIV-1 infection, Vaccine	human (A2.1)	Kundu1998a
	Vaccine *Vector/Type:* recombinant protein *Strain:* MN *HIV component:* gp160 • Ten HIV-1+ HLA A2 asymptomatic individuals were given two courses of HIV-1 MN rgp160 vaccine over a 2 year period • Two hundred and fifty three HIV-1 peptides of 9 or 10 aa possessing the HLA-A2.1 binding motif (Leu at position 2, Val at the C terminus) were identified in gp160, of which 25 had a high or intermediate binding affinity				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Eleven peptides were studied that had high HLA-A2 binding affinity – a CTL response was detected to 9/11 peptides in at least 1 individual • CTL responses after reimmunization may include recall responses – only individuals with vaccine cross-reactive sequences prior to vaccination showed detectable CTL responses				
gp160 (34–55)	gp120 (25–46 BRU)	LWVTVYYGVPVWKEATTTL-FCA	HIV-1 infection	human (A2)	Dadaglio1991
	• Defined through peptide blocking of CTL activity, and Env deletions				
gp160 (36–46)	gp120 (36–46 CM243 subtype CRF01)	VTVYYGVPVWR	HIV-1 exposed seronegative	human (A11)	Sriwanthana2001
	• Epitope name: E36-4 • This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand • HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed • This epitope after a second stimulation *in vitro* gave a weak response in HEPS study subject 186 who was HLA A2/A11				
gp160 (36–46)	gp120 (36–46 CM243 subtype CRF01)	VTVYYGVPVWR	HIV-1 infection	human (A11)	Bond2001
	• HLA-A11 CRF01 (called subtype E in Bond et al.) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive • 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 finding and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified • This epitope was not predicted by the EpiMatrix method to be likely to bind to A11, though it served as an epitope in the FSWs, and it was one of the six A11 epitopes that had been previously defined • 1/8 tested FSWs recognized this epitope • This epitope was only conserved in CRF01 and subtypes B and C, and exact matches were uncommon				
gp160 (36–46)	gp120	VTVYYGVPVWK	HIV-1 infection	human (A11 and A*6801)	Threlkeld1997
	• Study of the fine specificity of an A3-like-HLA-super-type epitope (the A3-super-type includes A*0301, A*1101, A*3101, A*3301, and A*6801) • The A3 super-type is characterized as a hydrophobic or hydroxyl containing anchor residue at position 2, and a positive charge in the C-term position • While most lines were specific, a promiscuous cloned CTL line was derived from an HIV+ donor that could recognize this epitope presented by either A11 or A*6801				
gp160 (37–46)	gp120 (37–46 LAI)	TVYYGVPVWK	Vaccine	human (A*0301)	Johnson1994b
	Vaccine *Vector/Type:* vaccinia *HIV component:* gp160 • Multiple CTL clones obtained from two vaccinees • C. Brander notes that this is an A*0301 epitope in the 1999 database				
gp160 (37–46)	gp120 (37–46 LAI)	TVYYGVPVWK	Vaccine	human (A*0301)	Brander2001
	Vaccine *Vector/Type:* vaccinia *HIV component:* gp160 • C. Brander notes this is an A*0301 epitope				
gp160 (37–46)	gp120	TVYYGVPVWK	HIV-1 infection, Vaccine	human (A*0301)	Hanke2000, Wee2002
	Vaccine *Vector/Type:* DNA prime with vaccinia MVA boost *Strain:* subtype A *HIV component:* p17, p24, polyepitope				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000]. • Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].				
gp160 (37–46)		TVYYGVPVWK	HIV-1 infection	human (A03)	Sabbaj2002b
	• Epitope name: Env-VK9 • Among HIV+ individuals who carried HLA A03, 0/20 (0%) recognized this epitope				
gp160 (37–46)	Env	TVYYGVPVWK	Vaccine	SJL/J HLA transgenic mice (A11)	Ishioka1999
	Vaccine *Vector/Type:* DNA *HIV component:* polyepitope • A minigene vaccine construct encoding 6 HLA 2.1 and 3 HLA A11 restricted CTL epitopes, the universal Th cell epitope PADRE (pan-DR epitope) and an ER translocating signal sequence was constructed • The epitopes were chosen for dominant recognition by CTLs during HBV and HIV infections in humans • HLA transgenic mice were used for quantitating in vivo immunogenicity of DNA vaccines encoding HLA-restricted CTL epitopes.				
gp160 (37–46)	gp120 (37–46)	TVYYGVPVWK	Vaccine	human (A3)	Carruth1999
	Vaccine *Vector/Type:* canarypox *Strain:* MN, LAI *HIV component:* gp120, gp41, Gag, Protease • The vaccine used was a live recombinant canarypox (CP) virus vaccine containing multiple HIV-1 genes (HIV-1 MN gp120, HIV-1 LAI gp41, HIV-1 LAI Gag, HIV-1 LAI protease) • CD4+ and CD8+ Gag and Env specific CTL responses were detected in only 1/5 vaccinated volunteers, and were not detectable 1 year after vaccination • CTL responses to epitopes SLYNTVATL and TVYYGVPVWK from HIV+ control patients were used as positive controls • The study explored why vaccinees were non-responsive – non-response was not due to inherent defects or differences in the ability of these individuals to process and present antigen				
gp160 (37–46)	gp120 (37–46 LAI)	TVYYGVPVWK	HIV-1 infection	human (A3)	Goulder1997e, Goulder1997a
	• Identical twin hemophiliac brothers were both infected with the same batch of factor VIII • One had a response to this epitope, the other did not • [Goulder1997a] is a review of immune escape that summarizes this study				
gp160 (37–46)	gp120 (36–45)	TVYYGVPVWK	HIV-1 infection	human (A3)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
gp160 (37–46)	gp120 (37–46)	TVYYGVPVWK	HIV-1 infection	human (A3)	Day2001
	• The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• All patients recognized at least 1 A3 epitope, up to 8 A3 epitopes, but none was clearly dominant				
gp160 (37–46)	Env (49–58)	TVYYGVPVWK	HIV-1 infection	human (A3 supertype)	Propato2001
	• Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus • This epitope can bind 3/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801)				
gp160 (37–46)	gp120 (38–41 LAI)	TVYYGVPVWK	Vaccine	human (A3.1)	Johnson1994a
	Vaccine *Vector/Type:* vaccinia *HIV component:* gp160 • Highly conserved epitope recognized by multiple CTL clones from vaccinee				
gp160 (37–46)	gp120 (37–46 LAI)	TVYYGVPVWK	Vaccine	human (A3.1)	Ferris1999, Hammond1995
	Vaccine *Vector/Type:* vaccinia *HIV component:* gp160 • This peptide can be processed for HLA-A3.1 presentation by TAP-1/2 independent and dependent pathways				
gp160 (37–46)	gp120 (37–46 LAI)	TVYYGVPVWK	HIV-1 infection	human (B*0301)	Wilson2000a
	• Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load was also found • All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39 • ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK • The subject with A*0201 had a moderatly strong response to SLYNTVATL • Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705 • No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL				
gp160 (38–48)	gp120 (45–55)	VYYGVPVWKEA	HIV-1 infection	human (Cw7)	Nehete1998a
	• Three long-term non-progressors and one asymptomatic HIV+ individual were studied and found to have HLA class I C-restricted CD8+ Env-specific CTLs – Cw7 specific CTL were found against three peptides, including this one • HLA-C antigens are expressed on lymphoid cells to a lesser extent than either HLA-A or -B • HLA-C confers protection against lysis by natural killer cells and by non-MHC-restricted effector T cells and Cw7 directly governs this resistance to lysis – the authors hypothesize that pathogens that inhibit antigen expression and class I expression may particularly down regulate Cw7, thus triggering non-MHC restricted killing				
gp160 (42–51)	gp120 (42–51 PV22)	VPVWKEATTT	HIV-1 infection	human (B*5501)	Brander2001
	• C. Brander notes this is a B*5501 epitope				
gp160 (42–51)	gp120 (42–51 PV22)	VPVWKEATTT	HIV-1 infection	human (B55)	Brander1995b
	• P. Johnson, unpublished				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (42–51)	gp120 (41–55)	VPVWKEATTT	HIV-1 infection	human (B55)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
gp160 (42–52)	Env (43–52 BH10, LAI)	VPVWKEATTTL	HIV-1 infection	human	Maksiutov2002
	• This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins. • This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this peptide is PVWKEATTTL) has similarity with the platelet membrane glycoprotein IIIA precursor (GLIIIA) (integrin beta-3) (CD61): PLYKEATSTF.				
gp160 (42–52)	gp120 (42–52)	VPVWKEATTTL	HIV-1 infection	human (B*3501)	Brander2001
	• C. Brander notes this is a B*3501 epitope				
gp160 (42–52)	gp120 (42–52 PV22)	VPVWKEATTTL	HIV-1 infection	human (B35)	Cao1997a
	• VPVWKEATTTL is the consensus sequence for clades B and D • VPVWKDAETTL is the consensus sequence for clade A and it is cross-reactive • VPVWKEADTTL is the consensus sequence for clade C and it is cross-reactive • VPVWKEADTTL is the consensus sequence for clade E and even with three substitutions still retains some cross-reactivity				
gp160 (42–52)	gp120 (41–51)	VPVWKEATTTL	HIV-1 infection	human (B35)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
gp160 (42–61)	gp120 (49–68)	VPVWKEATTTLFCASDAKAY	HIV-1 infection	human	Lieberman1995
	• HIV-specific CTL lines developed by ex vivo stimulation with peptide				
gp160 (42–61)	gp120 (49–68 SF2)	VPVWKEATTTLFCASDAKAY	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • Eleven subjects had CTL that could recognize vaccinia-expressed LAI gp160 • Three of these 11 had CTL response to this peptide • The responding subjects were HLA-A2, A3, B8, B62; HLA-A3, A24, B7, B38				
gp160 (42–61)	gp120 (49–68 SF2)	VPVWKEATTTLFCASDAKAY	HIV-1 infection	human	Lieberman1997b
	• CTL expanded ex vivo were later infused into HIV-1 infected patients				
gp160 (50–59)	Env (62–71)	TTLFCASDAK	HIV-1 infection	human (A3 supertype)	Propato2001
	• Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus • This epitope can bind 3/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801)				
gp160 (51–59)	Env (63–71)	TLFCASDAK	HIV-1 infection	human (A3 supertype)	Propato2001
	• Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus • This epitope can bind 3/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801)				
gp160 (52–61)	gp120 (59–68 HXB2)	LFCASDAKAY	HIV-1 infection	human (A*2402)	Lieberman1992
	• CTL epitope defined by T cell line and peptide mapping • C. Brander notes that this is an A*2402 epitope in the 1999 database				
gp160 (52–61)	gp120 (53–62 LAI)	LFCASDAKAY	HIV-1 infection	human (A*2402)	Brander2001
	• C. Brander notes this is an A*2402 epitope				
gp160 (52–61)	gp120 (53–62)	LFCASDAKAY	HIV-1 infection, HIV-1 exposed seronegative	human (A24)	Kaul2001a
	• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers				
gp160 (52–61)	gp120 (53–62 LAI)	LFCASCAKAY	HIV-1 infection	human (B38)	Shankar1996
	• Uncertain whether optimal, binds A24 as well				
gp160 (52–71)	gp120 (59–78)	LFCASDAKAYDTEVHINVW-AT	HIV-1 infection	human	Lieberman1995
	• HIV-specific CTL lines developed by ex vivo stimulation with peptide				
gp160 (52–71)	gp120 (59–78 SF2)	LFCASDAKAYDTEVHINVW-AT	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • Eleven subjects had CTL that could recognize vaccinia-expressed LAI gp160 • One of these 11 had CTL response to this peptide • The responding subject was HLA-A2 and B-21				
gp160 (62–80)	gp120 (69–88 SF2)	DTEVHNVWATHACVPTDPN	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • Eleven subjects had CTL that could recognize vaccinia-expressed LAI gp160 • One of these 11 had CTL response to this peptide • The responding subject was HLA-A2 and B-21				
gp160 (78–86)	gp120 (77–85)	DPNPQEVVL	HIV-1 infection	human (B*3501)	Ogg1998b
	• This epitope was included to illustrate the specificity of HIV-tetrameric staining, in a cross-sectional study correlating HLA A*0201 CTL effector cells and low viral load				
gp160 (78–86)	gp120 (77–85 SF2)	DPNPQEVVL	HIV-1 infection	human (B*3501)	Brander2001
	• C. Brander notes this is a B*3501 epitope				
gp160 (78–86)	gp120 (77–85 SF2)	DPNPQEVVL	HIV-1 infection	human (B*3501)	Tomiyama1997
	• A CTL clone responsive to this epitope was obtained • 2/7 B35-positive individuals have a CTL response to this epitope • This epitope is highly variable				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The substitutions: 1N, 3S and 7I, 7L and 9M, 8I, 8K all abrogate specific CTL lysis, while only 8K reduces binding to B*3501 • The substitution 8V to 8E does not reduce specific CTL activity				
gp160 (78–86)	Env (77–85)	DPNPQEVVL	HIV-1 infection	human (B*3501)	Ogg1999
	• CTL effector levels were measured after potent ARV therapy using HLA-tetramer complexes for the A*0201 epitopes SYLVANTVATL and ILKEPVHGV in seven patients, and the B*3501 epitope DPNPQEVVL in one additional patient • Levels of CTL effectors typically decline for 5-7 days and then rebound, fluctuating during the first two weeks of therapy • After the early fluctuation, there was a steady exponential decay with a median half-life of 45 days				
gp160 (78–86)	Env (77–85)	DPNPQEVVL	HIV-1 infection	human (B35)	Dyer1999
	• CTL specific responses were measured over a 1.3 to 1.5 year period in members of the Sydney Blood Bank Cohort (SBBC) who had been infected with a natural attenuated strain of HIV-1 which was Nef-defective • Some of these patients had prolonged high levels of CTL effector and memory cells despite low viral load				
gp160 (78–86)		DPNPQEVVL	HIV-1 infection	human (B35)	Wilson2000a
	• Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load was also found • All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39 • ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK • The subject with A*0201 had a moderatly strong response to SLYNTVATL • Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705 • No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL				
gp160 (78–86)	(SF2)	DPNPQEVVL	HIV-1 infection	human (B35)	Kawana1999
	• HLA B35 is associated with rapid disease progression • The sequences of 9 previously described HIV-1 B35 CTL epitopes were obtained in 10 HLA B35+ and 19 HLA B35- individuals • 3/9 CTL epitopes had substitutions that were more common in B35+ individuals than in B35- individuals, but this was one of the six that had no B35 associated pattern of mutation				
gp160 (78–86)	gp120 (77–85 SF2)	DPNPQEVVL	HIV-1 infection	human (B35)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-B35+ individuals that had a CTL response to this epitope broken down by group: 1/2 group 1, 0/2 group 2, and 0/1 group 3				
gp160 (78–86)		DPNPQEVVL	HIV-1 infection	human (B35)	Sabbaj2002b
	• Epitope name: Env-DL9				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Among HIV+ individuals who carried HLA B35, 3/20 (15%) recognized this epitope				
gp160 (78–86)	gp120 (77–85 SF2)	DPNPQEVVL	HIV-1 infection	human (B35, B51)	Shiga1996
	• Binds HLA-B*3501 and B*5101 – binds and kills gp120-vaccinia virus infected cells carrying B35 or B51				
gp160 (78–86)	gp120 (77–85)	DPNPQEVVL	HIV-1 infection, HIV-1 exposed seronegative	human (B51)	Kaul2001a
	• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers				
gp160 (103–111)	Env (102–110)	QMHEDIISL	HIV-1 infection	human (A*0201)	Kmieciak1998a
	• CTL responses in six patients to four Env epitopes were studied: D2: LLNATAIAV, 5.3: RLRDLLLIV, D1: KLTPLCVTL, and 4.3: QMHEDIISL – all have A2 anchor residues; • The C terminal epitopes (D2 and 5.3) were highly variable and the variability was considered responsible for limited CTL response, while D1 and 4.3, N-terminal epitopes, were much more conserved and gave evidence of high levels of CTL response in vitro; • Peptides 4.3 and D1 bound HLA-A*0201 molecules with high affinity; • Peptides 4.3 and D1 stimulated CTL with a relatively limited TCR Vbeta repertoire;				
gp160 (104–119)	gp120 (111–126 IIIB)	MQEDIISLWDQSLKPC	in vitro stimulation	human	Macatonia1991
	• Primary CTL response with cells from non-infected donors stimulated by the peptide				
gp160 (105–117)	gp120 (MN)	HEDIISLWDQSLK	HIV-1 infection	chimpanzee	Lubeck1997
	• No epitope-specific CTL were detected in chimpanzees immunized with adenovirus-HIV-1 MN gp160 recombinant despite a response to peptides P18 and T1 • Helper and cytotoxic T cells have been found to be stimulated by this peptide (T2)				
gp160 (105–117)	gp120 (112–124 IIIB)	HEDIISLWDQSLK	HIV-1 exposed seronegative	human	Pinto1995
	• CTL and T helper cell reactivity in healthcare workers exposed to HIV				
gp160 (105–117)	gp120 (112–124 IIIB)	HEDIISLWDQSLK	HIV-1 infection	human (A2)	Clerici1991a
	• Helper and cytotoxic T cells can be stimulated by this peptide (T2)				
gp160 (108–116)	Env (107–115 subtype B)	IISLWDQSL	Vaccine	human (A2.1)	Kundu1998a
	Vaccine *Vector/Type:* recombinant protein *Strain:* MN *HIV component:* gp160 • Ten HIV-1+ HLA A2 asymptomatic individuals were given two courses of HIV-1 MN rgp160 vaccine over a 2 year period • Two hundred and fifty three HIV-1 peptides of 9 or 10 aa possessing the HLA-A2.1 binding motif (Leu at position 2, Val at the C terminus) were identified in gp160, of which 25 had a high or intermediate binding affinity • Eleven peptides were studied that had high HLA-A2 binding affinity – a CTL response was detected to 9/11 peptides in at least 1 individual • CTL responses after reimmunization may include recall responses – only individuals with vaccine cross-reactive sequences prior to vaccination showed detectable CTL responses				
gp160 (109–117)	Env (109–117 CM243 subtype CRF01)	ISLWDQSLK	HIV-1 exposed seronegative	human (A11)	Bond2001
	• Epitope name: E109-117 • This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed • This epitope was weakly reactive in the HEPS study subject 265 who was HLA A2/A11, and had been predicted to be a possible A11 epitope using Epimer in [Bond2001]				
gp160 (112–130)	gp120 (119–139 SF2)	WDQSLKPCVKLTPLCVSLK	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • Eleven subjects had CTL that could recognize vaccinia-expressed LAI gp160 • One of these 11 had CTL response to this peptide • The responding subject was HLA-A2 and B-21				
gp160 (117–126)	Env (72–81)	KPCVKLTPLC	HIV-1 infection	human (B7)	Jin2000b
	• This B7 epitope is one of three subdominant CTL responses detected in a long-term non-progressor • A dominant B7 epitope was defined using conventional methods, and three additional sub-dominant HLA B7 epitopes were defined by first using a non-anchor based strategy, EpiMatrix, to identify 2078 possible epitopes in the autologous HIV-1, followed by B7 anchor residue prediction to narrow the set to 55 peptides for experimental testing				
gp160 (121–129)	Env (120–128)	KLTPLCVTL	HIV-1 infection	human (A*0201)	Kmieciak1998a
	• CTL responses in six patients to four Env epitopes were studied: D2: LLNATAIAV, 5.3: RLRDLLLIV, D1: KLTPLCVTL, and 4.3: QMHEDIISL—all have A2 anchor residues • The C terminal epitopes (D2 and 5.3) were highly variable and the variability was considered responsible for limited CTL response, while D1 and 4.3, N-terminal epitopes, were much more conserved and gave evidence of high levels of CTL response in vitro • Peptides 4.3 and D1 bound HLA-A*0201 molecules with high affinity • Peptides 4.3 and D1 stimulated CTL with a relatively limited TCR Vβ repertoire • In a longitudinal study, the CTL response to the variable D2 epitope diminished over time, while the response to the conserved epitope D1 stayed higher over time				
gp160 (121–129)	Env (134–)	KLTPLCVTL	HIV-1 infection	human (A*0201)	Altfeld2001c
	• Epitope name: Env-134 • HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested • Three additional previously described HLA-A2 epitopes were added to the set of 20, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acute infected individuals recognized at least 1 (median of 1 and maximum of 2) • 2/22 individuals with chronic HIV-1 infection recognized this epitope in ELISPOT • 0/12 acutely infected individuals recognized this epitope • KLTPLCVTL binds to four HLA-A2 supertype alleles: A*0201, A*0202, A*0203 and A*6802 (highest affinity).				
gp160 (121–129)	gp120 (120–128 LAI)	KLTPLCVTL	Vaccine	human (A2)	Dupuis1995
	Vaccine *Vector/Type:* recombinant protein *Strain:* MN *HIV component:* gp160 • CTL from HLA-A2 positive subject react with this peptide				
gp160 (121–129)	gp120 (120–128)	KLTPLCVTL	Vaccine	human (A2)	Woodberry1999
	Vaccine *Vector/Type:* vaccinia *HIV component:* polyepitope • A polyepitope vaccine was generated in a vaccinia construct that contiguously encoded seven epitopes, all presented by HLA A-2				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• HHD mice have a transgene of HLA A2 linked to the transmembrane and cytotoxic domains of H-2D^d – this transgene is the only MHC molecule expressed in the mice • CTL responses to Gag (77-85) SLYNTVATL, Pol (476-484) ILKEPVHGV, gp120 (120-128) KLTPLCVTL, and Nef (190-198) AFHHVAREL were observed in HIV polytope HHD-vaccinated mice, and these responses were enhanced with vaccinia boost • No CTL immune responses were generated against HLA A2-restricted HIV epitopes Nef 157-166 (PLTFGWCYKL), Pol 346-354 (VIYQYMDDL), and Nef 180-189 (VLEWRFDSRL) • Sixteen HLA A2+ patients were tested for their ability to make CTL responses by peptide restimulation in culture with the epitopes selected for inclusion in the polytope – one individual recognized all seven of these epitopes; 7 patients had CTL cultures able to recognize at least one of the epitopes, and 6 of those 7 recognized more than one epitope, but they were not able to test all peptides for all patients; many patients only had three peptides tested • KLTPLCVTL was recognized by 3 of the patients				
gp160 (121–129)	gp120 (120–128)	KLTPLCVTL	HIV-1 infection	human (A2)	Kundu1998b
	• Allogeneic dendritic cells (DCs) were obtained from HLA-identical siblings, pulsed with rgp160 MN or A2-restricted HIV-1 epitope peptides, and infused monthly into six HIV-infected patients • 1/6 showed increased env-specific CTL and increased lymphoproliferative responses, 2/6 showed increase only in proliferative responses, and 3/6 showed no change – pulsed DCs were well tolerated • KLTPLCVTL is a conserved HLA-A2 epitope included in this study – all six patients had this sequence as their HIV direct sequence, and a detectable CTL response • CTL demonstrated against peptide-coated target, epitope is naturally processed and enhancible with vaccine				
gp160 (121–129)	gp120 (120–128)	KLTPLCVTL	HIV-1 infection	human (A2)	Kmieciak1998b
	• Increased CTL response to cells expressing a VV construct Δv3 mutant compared with a full-length env gene product				
gp160 (121–129)	gp120 (121–129)	KLTPLCVSL	in vitro stimulation	human (A2)	Zarling1999
	• This study compares the ability of macrophages and dendritic cells to stimulate primary responses in CD8+ lymphocytes isolated from HLA-appropriate HIV-uninfected donors using peptide-pulsed APC – the dendritic cells performed better as APC for the stimulation of primary responses • Strong CTL responses were elicited by the epitopes DRFYKTLRA and GEIYKRWII when presented by either immature or mature dendritic cells – macrophages were not able to prime a CTL response against DRFYKTLRA • A weak response to KLTPLCVSL was stimulated using macrophages as the APC • No detectable response was observed for the following previously-defined HIV epitopes: KIRLRPGGK, ILKEPVHGV, IRLRPGGK, GPKVKQWPL				
gp160 (121–129)	gp120 (120–128)	KTLPLCVTL	HIV-1 infection	human (A2)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
gp160 (121–129)	gp120 (121–129 IIIB)	KLTPLCVTL	Vaccine	murine (A2)	Kiszka2002
	Vaccine *Vector/Type:* DNA, DNA with recombinant protein boost *Strain:* IIIB *HIV component:* gp160, gp160deltaV3 *Adjuvant:* IL-12 (IL-12p35 and IL-12p40) • Epitope name: D1 • Transgenic mice expressing a HLA-A2/Kb chimeric protein were vaccinated with a full length gp160 or with gp160deltaV3, with the V3 loop deleted. Mice given gp160deltaV3 had a broader immune response than those given gp160, with increased responses to conserved HLA-A2 epitopes in the C1 region of gp120, KLTPLCVTL, and the C-term region of gp41, SLLNATAIAV. • Greater resistance was conferred by the gp160deltaV3 than the gp160 vaccine to a challenge of vaccinia expressing heterologous gp160 from primary isolates (VI-06 and 89.6), and the resistance was conferred by CD8+ T-cells.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (121–129)	Env (134–142)	KLTPLCVTL	HIV-1 infection	human (A2 supertype)	Propato2001
	• Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus • This epitope can bind four of the five HLA-A2 supertypes alleles (A*0201, A*020 2, A*0203, A*0206 and A*6802)				
gp160 (121–129)	Env	KLTPLCVTL	Vaccine	SJL/J HLA transgenic mice (A2.1)	Ishioka1999
	Vaccine *Vector/Type:* DNA *HIV component:* polyepitope • A minigene vaccine construct encoding 6 HLA 2.1 and 3 HLA A11 restricted CTL epitopes, the universal Th cell epitope PADRE (pan-DR epitope) and an ER translocating signal sequence was constructed • The epitopes were chosen for dominant recognition by CTLs during HBV and HIV infections in humans • HLA transgenic mice were used for quantitating in vivo immunogenicity of DNA vaccines encoding HLA-restricted CTL epitopes – strong responses were observed to all nine epitopes, and CTL memory persisted up to four months after a single injection				
gp160 (121–129)	Env (120–128 subtype B)	KLTPLCVTL	Vaccine	human (A2.1)	Kundu1998a
	Vaccine *Vector/Type:* recombinant protein *Strain:* MN *HIV component:* gp160 • Ten HIV-1+ HLA A2 asymptomatic individuals were given two courses of HIV-1 MN rgp160 vaccine over a 2 year period • Two hundred and fifty three HIV-1 peptides of 9 or 10 aa possessing the HLA-A2.1 binding motif (Leu at position 2, Val at the C terminus) were identified in gp160, of which 25 had a high or intermediate binding affinity • Eleven peptides were studied that had high HLA-A2 binding affinity – a CTL response was detected to 9/11 peptides in at least 1 individual • CTL responses after reimmunization may include recall responses – only individuals with vaccine cross-reactive sequences prior to vaccination showed detectable CTL responses				
gp160 (156–165)	Env (162–171 BH10, LAI)	NCSFNISTSI	HIV-1 infection	human	Maksiutov2002
	• This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins. • This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is STSIRGKVQK) has similarity with the macrophage colony stimulating factor I receptor fragment SISIRLKVQK.				
gp160 (156–165)	gp120 (156–165)	NCSFNISTSI	HIV-1 infection	human (Cw*08)	Ferris1999
	• Recognized by CTL clone LWF A5, isolated from a lab worker exposed to HIV-1 in 1985 • The processing of this epitope is TAP1/2-dependent, as are most Env epitopes, and it contains two N-linked glycosylation sites that are glycosylated in Env • Only peptide that has been deglycosylated, a process that changes asparagine (N) to aspartic acid (D) was recognized: the aspartic acid at position 5 was critical, position 1 could be either D or N • This peptide also contains a Cys involved in a disulfide linkage but reducing conditions did not effect recognition by CTL clone LWF A5 • The HIV-1 Env epitopes are typically processed by a TAP1/2 dependent mechanism, which involves cotranslational translocation into the ER, glycosylation, export back into the cytosol, and deglycosylation for processing, and retransport into the ER for the association with class I molecules • The particular pathway of generating an epitope may have an impact on the presentation of that epitope, quantitatively as well as qualitatively				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (156–165)	gp120 (156–165 IIIB)	NCSFNISTSI	HIV-1 infection	human (Cw8)	Sipsas1997
	• HIV IIIB proteins were used to define the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB • NCSFNITTSI, a variant found in HIV-1 MN, was not recognized, thus this epitope was type-specific • NCSFNISTSI contains two potential N-linked glycosylation sites and cysteine residue, possibly related to the requirement for a high sensitizing dose of peptide for CTL activity				
gp160 (188–207)	gp120 (193–212 BRU)	TTSYTLTSCNTSVITQACPK	HIV-1 infection	human (A2)	Dadaglio1991
	• Defined through blocking CTL activity, and Env deletions				
gp160 (191–200)	gp120 (194–202 CM243 subtype CRF01)	YRLINCNTSV	HIV-1 infection	human (A2)	Sriwanthana2001
	• Epitope name: E191-200 • This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand • HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed • This epitope was reactive in HIV+ control study subject 144 who carried HLA-A2				
gp160 (191–200)	gp120 (194–202 CM243 subtype CRF01)	YRLINCNTSV	HIV-1 infection	human (A2)	Bond2001
	• More than half of a cohort of HIV+ female sex workers (FSW) from Northern Thailand were HLA-A11 positive, and this study concentrated on A11 epitopes in this group, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested. • 1/4 tested FSWs recognized the E clade version of this epitope, which differs from the previously defined B clade version by four amino acids, KLTSCNTSV • This epitope was somewhat conserved in 4/8 subtypes: CRF01 (E), B, C, and D				
gp160 (192–200)	gp120 (192–199)	KLTSCNTSV	HIV-1 infection	human (A*02)	Rinaldo2000
	• Epitope name: SL9 • Administration of triple-drug antiretroviral therapy (IDV, 3TC and ZDV) sometimes showed a transient increase and other times failed to increase CTL responses in patients with advanced HIV disease, but there is a stable population of tetramer stained HIV-specific CD8+ CD45RO+ cells that persist after therapy and long periods of virus being below the level of detection				
gp160 (192–200)	gp120 (192–199 HXB2R)	KLTSCNTSV	HIV-1 infection	human (A2)	Brander1995a
	• Epitope predicted on HLA binding motif, and studied in the context of inclusion in a synthetic vaccine				
gp160 (192–200)	gp120 (192–199)	KLTSCNTSV	HIV-1 infection	human (A2)	Huang2000
	• The single cell ELISPOT assay was optimized and highly specific, and found to work well even after the primary cells had been frozen and thawed • Increases in gamma interferon producing cells were observed in response to anti-retroviral therapy using single cell IFN-gamma-production ELISPOT				
gp160 (192–200)	gp120 (197–205)	TLTSCNTSV	Peptide-HLA interaction	human (A2)	Garboczi1992
	• Crystallization of HLA-A2 molecules complexed with antigenic peptides – refers to Dadaglio et al 1991				
gp160 (192–200)	gp120 (199–207)	TLTSCNTSV	HIV-1 infection	human (A2.1)	Brander1996a
	• This epitope was recognized by PBMC from 6/14 HIV+ asymptomatic patients • This epitope was used along with pol CTL epitope ALQDSGLEV and a tetanus toxin T helper epitope for a synthetic vaccine				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This vaccine failed to induce a CTL response, although a helper response was evident				
gp160 (192–211)	gp120 (199–219 SF2)	SLTSCNTSVITQACPKVSFE	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • Eleven subjects had CTL that could recognize vaccinia-expressed LAI gp160 • One of these 11 had CTL response to this peptide • The responding subject was HLA-A2, -B21				
gp160 (199–207)	Env (202–210)	SVITQACPK	HIV-1 infection	human (A*1101)	Fukada2002
	• Counterparts for eight known clade B HLA A*1101 epitopes were generated for clade E (CRF01). Three epitopes, identical among clade A-E, were cross-reactive and recognized by clade E infected individuals. The clade E and B analogs to three more HLA A*1101 epitopes was recognized in a clade specific manner. Two other HLA A*1101 clade B defined epitopes were found not to have stimulated a response in clade E infected individuals. • SVITQACPK was found to elicit clade-specific responses in clade B (SVITQACPK is most common, sAitqacpk is most common variant in clade A, C and D) and clade E (saiKqacpk is most common). SVITQACPK was recognized by CTL from 3/5 B clade infected Japanese subjects, and aiKqacpk by CTL from 0/7 E clade infected Thai subjects, so this seems to be a B clade exclusive epitope. • The binding of the three variant peptides to HLA A*1101 was comparable, implicating TCR interaction differences.				
gp160 (201–225)	gp120 (201–225 LAI)	ITQACPKVSFEPIPHYCAP-AGFAI	Vaccine	human (CD4+ CTL)	Johnson1994b, Johnson1994a
	Vaccine *Vector/Type:* vaccinia *HIV component:* gp160 • CD4+ CTL isolated from LAI IIIB gp160 vaccinees				
gp160 (202–221)	gp120 (209–228)	TQACPKVSFEPIPIHYCAPA	HIV-1 infection	human	Lieberman1995
	• HIV-specific CTL lines developed by ex vivo stimulation with peptide				
gp160 (202–221)	gp120	TQACPKVSFEPIPIHYCAPA	HIV-1 infection	human	Weekes1999b
	• Peptide 740.18: Almost all CD8+ T cells are CD28+ at birth, and the proportion of CD28-CD8+ cells increases with age – this study examines the contribution of CD8+CD28- cells to CTL memory pools for CTL clones specific for two persistent human viruses, CMV and HIV – clones were found to be similarly distributed the CD28 depleted cell population • HIV CTL responses to 3 Env and 2 Gag peptides were studied • The clonal composition of the TCR Vbeta responses were studied and was found to be highly focused, with one TCR beta-chain sequence tending to dominate the peptide-specific response – clones to this epitope were Vbeta13.1				
gp160 (202–221)	gp120	TQACPKVSFEPIPIHYCAPA	HIV-1 infection	human	Weekes1999a
	• Peptide 740.18: Memory CTL specific for HIV-1 may contribute to oligoclonal expansions within the CD57+ CD28- CD8+ CTLp populations				
gp160 (202–221)	gp120 (209–228 SF2)	TQACPKVSFEPIPIHYCAPA	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • Eleven subjects had CTL that could recognize vaccinia-expressed LAI gp160 • One of these 11 had CTL response to this peptide				
gp160 (202–221)	gp120 (209–228 SF2)	TQACPKVSFEPIPIHYCAPA	HIV-1 infection	human	Lieberman1997b
	• CTL expanded ex vivo were later infused into HIV-1 infected patients				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (207–216)	gp120 (subtype A)	KMTFEPIPIH	HIV-1 infection	human (A29)	Cao2000
	• HIV-1 subtypes A and D dominate the Ugandan epidemic, and a vaccine trial using B clade antigen is underway – this study addresses relative levels of cross-reactive CTL responses in Ugandans to A, D, and B clade recombinant vaccinia viruses expressing Gag, Env, Pol, RT or Nef from HIV-1 clades A, B, and D • Proteins corresponding to the subtype of the infecting strains tended to trigger higher levels of CTL response measured by percent specific lysis, but there was extensive inter-subtype cross-reactivity with B clade proteins and the co-circulating subtype • CTL derived from subtype A clade infection (patient SP 528), recognized the subtype A version of the peptide (KMSFEPIPIH), had a slightly reduced specific lysis using the B clade version of the peptide (KVSFEPIPIH), and no lysis using the D clade version of the epitope (KVTFEPIPIH) • Patient SP 528 is HLA A1, A29, B57, B81, Bw4, Bw6			
gp160 (208–217)	gp120 (subtype B)	VSFEPIPIHY	HIV-1 exposed seronegative	human (A29)	Kaul2000
	• 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 gamma-IFN responses in the cervix – systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses • Low risk individuals did not have such CD8+ cells • CD8+ T cell epitopes: DTVLEDINL (3 individuals), SLYNVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women			
gp160 (208–217)	gp120 (263–272)	VSFEPIPHY	HIV-1 infection, HIV-1 exposed seronegative	human (A29)	Kaul2001a
	• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers				
gp160 (208–219)	Env	VSFEPIPPHYCA	HIV-1 infection	human (A2)	Cao2002
	• SP 511 is an A2 restricted CTL clone generated from a Ugandan subject that recognizes VSFEPIPPHYCA. • CTL could be activated by a fusion protein of an HIV protein and anthrax lethal factor (LFn-HIV) that promotes antigen presenting cell uptake of exogenous protein and allows processing through the MHC class I pathway. This strategy for CTL detection could allow antigen presentation without generation of cells by the standard methods of using live viral vectors carrying a protein, or by loading the cells with peptides and by-passing processing.				
gp160 (209–217)	(LAI)	SFEPIPIHY		(A29)	Altfeld2000a, Brander2001
gp160 (209–217)	gp120 (213–221 SF2)	SFEPIPIHY	HIV-1 infection	human (A29)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-A29+ individuals that had a CTL response to this epitope broken down by group: 1/3 group 1, 0/0 group 2, and 0/0 group 3				
gp160 (212–231)	gp120	PIPIHYCAPAGFAILKCNNK	HIV-1 infection	human	Weekes1999a
	• Peptide 740.19: Memory CTL specific for HIV-1 may contribute to oligoclonal expansions within the CD57+ CD28- CD8+ CTLp populations				
gp160 (212–231)	gp120 (219–238 HXB2)	PIPIHYCAPAGFAILKCNNK	HIV-1 infection	human	Lieberman1992
	• CTL epitope defined by T cell line and peptide mapping				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (212–231)	gp120 (219–238)	PIPIHYCAPAGFAILKCNNK	HIV-1 infection	human	Lieberman1995
	• HIV-specific CTL lines developed by ex vivo stimulation with peptide				
gp160 (212–231)	gp120	PIPIHYCAPAGFAILKCNNK	HIV-1 infection	human (A2)	Weekes1999b
	• Peptide 740.19: Almost all CD8+ T cells are CD28+ at birth, and the proportion of CD28-CD8+ cells increases with age – this study examines the contribution of CD8+CD28- cells to CTL memory pools for CTL clones specific for two persistent human viruses, CMV and HIV – clones were found to be similarly distributed in the CD28 depleted cell population • HIV CTL responses to 3 Env and 2 Gag peptides were studied • The clonal composition of the TCR Vbeta responses was studied and was found to be highly focused, with one TCR beta-chain sequence tending to dominate the peptide-specific response – clones to this epitope were Vbeta13.6				
gp160 (212–231)	gp120	PIPIHYCAPAGFAILKCNNK	HIV-1 infection	human (B57)	Jin1998b
	• Progressive HIV-1 infection and CD4 decline was associated decreased the IL-2-expandable HIV-1 CTL response in 10 asymptomatic HIV-infected patients – this observation may be partially due to a reduction and impaired function of T helper cells, CTL exhaustion and APC dysfunction • Continued presence of HIV-1 specific memory cells (CTLp) was observed in three patients, one to GIWGCSGKLICTTAV, one to ALIWEDLRSLCLFSY, and one to PIPIHYCAPAGFAILKCNNK				
gp160 (237–246)	Env	GPCKNVSTVQ		human (B56)	De Groot2001
	• The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes • A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes were identified that could stimulate IFNγ production in an ELISPOT assay • GPCKNVSTVQ was newly defined as an epitope in this study, was shown to stimulate an ELISPOT response, and to bind to HLA-B7				
gp160 (239–247)	gp120 (241–249 LAI)	CTNVSTVQC	HIV-1 infection	human (Cw8)	Sipsas1997
	• HIV IIIB proteins were used to define the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB • CTNVSTVQC contains a potential N-linked glycosylation site and cysteine residues, possibly related to a requirement for a high sensitizing dose of peptide for CTL activity				
gp160 (242–261)	gp120 (249–268)	VSTVQCTHGIRPVVSTQLLL	HIV-1 infection	human	Lieberman1995
	• HIV-specific CTL lines developed by ex vivo stimulation with peptide				
gp160 (242–261)	gp120 (249–268 SF2)	VSTVQCTHGIRPVVSTQLLL	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • Eleven subjects had CTL that could recognize vaccinia-expressed LAI gp160 • One of these 11 had CTL response to this peptide • The responding subject was HLA-2, -B21				
gp160 (242–261)	gp120 (249–268)	VSTVQCTHGIRPVVSTQLLL	HIV-1 infection	human	Lieberman1997b
	• CTL expanded ex vivo were later infused into HIV-1 infected patients				
gp160 (252–260)	gp120 (255–263 SF2)	RPIVSTQLL	HIV-1 infection	human (B*3501)	Tomiyama1997
	• A CTL clone responsive to this epitope was obtained • Only 1/7 B35-positive individuals had a CTL response to this epitope • An I to V substitution at position 3 reduces specific lysis, but not binding to B*3501 • A Q to H substitution at position 7 abrogates specific lysis, but not binding to B*3501				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (252–260)	gp120 (255–263 SF2) • Binds HLA-B*3501	RPIVSTQLL	HIV-1 infection	human (B35)	Shiga1996
gp160 (252–260)	(SF2) • HLA B35 is associated with rapid disease progression • The sequences of 9 previously described HIV-1 B35 CTL epitopes were obtained in 10 HLA B35+ and 19 HLA B35- individuals • 3/9 CTL epitopes had substitutions that were more common in B35+ individuals than in B35- individuals, but this was one of the six that had no B35 associated pattern of mutation	RPIVSTQLL	HIV-1 infection	human (B35)	Kawana1999
gp160 (252–261)	Env • The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes • A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 of the predicted B7 superfamily (HLA B7, B8, and B58) epitopes were identified that could stimulate IFNγ production in an ELISPOT assay • RPVVSTQLLL was one of the 15, and had been previously identified as an HLA-B7 epitope, and was confirmed in this study	RPVVSTQLLL		human (B7)	De Groot2001
gp160 (252–271)	Env (256–268 BH10, LAI) • This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins. • This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is STQLLLNGSLAEE) has similarity with the lymphatic endothelium-specific hyaluronan receptor LYVE-1 fragment TTRLLVQGSLRAEE.	RPVVSTQLLLNGSLAEEEVV	HIV-1 infection	human	Maksiutov2002
gp160 (252–271)	gp120 (256–275 LAI)	RPVVSTQLLLNGSLAEEEVV	HIV-1 infection	human (B7)	Shankar1996
gp160 (291–307)	Env (292–301 BH10, LAI) • This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins. • This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is VEINCTRPNN) has similarity with the FasI receptor precursor (Apptosis-mediating surface antigen fas) (APO-1 antigen) (CD95 antigen) fragment VEINCTRQN.	SVEINCTRPNNNTRKSI	HIV-1 infection	human	Maksiutov2002
gp160 (291–307)	gp120 (295–312 BRU) • Defined through blocking CTL activity, and Env deletions	SVEINCTRPNNNTRKSI	HIV-1 infection	human (A2)	Dadaglio1991
gp160 (291–307)	gp120 (291–307 IIIB) **Vaccine** *Vector/Type:* DNA, DNA with recombinant protein boost *Strain:* IIIB *HIV component:* gp160 *Adjuvant:* IL-12 (IL-12p35 and IL-12p40) • Transgenic mice expressing a HLA-A2/Kb chimeric protein were vaccinated with a full length gp160 or with gp160deltaV3, with the V3 loop deleted. Mice given gp160deltaV3 had a broader immune response than those given gp160, with increased responses to conserved HLA-A2 epitopes in the C1 region of gp120, KLTPLCVTL, and the C-term region of gp41, SLLNATAIAV. • Greater resistance was conferred by the gp160deltaV3 than the gp160 vaccine to a challenge of vaccinia expressing heterologous gp160 from primary isolates (VI-06 and 89.6), and the resistance was conferred by CD8+ T-cells. • The most intense CTL responses to the intact gp160 vaccine were directed at three V3 peptides.	SVEINCTRPNNNTRKRI	Vaccine	murine (A2)	Kiszka2002
gp160 (297–322)	gp120 (297–322 IIIB) **Vaccine** *Vector/Type:* peptide *Strain:* IIIB *HIV component:* V3 *Adjuvant:* liposome • Induction of peptide-specific CTLs in BALB/c mice was dependent on immunization with peptide encapsulated liposomes containing MPL as adjuvant	TRPNNNTRKRIRIQRGPGR-AFVTIGK	Vaccine	murine (H-2D^d)	Chang1999

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• T26K (26mer) elicited a stronger AB and CTL response than R15K (a V3 15mer, RIQRGPGRAFVTIGK)				
gp160 (297–330)	Env (303–335 BX08)	TRPNNNTRKSIHIGPGRAF-YATGEIIGDIRQAH	Vaccine	human	Gahery-Segard2000
	Vaccine *Vector/Type:* lipopeptide *HIV component:* six peptides • Anti-HIV lipopeptide vaccine consisting of six long amino acid peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial • A CD4+ T cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 6/10 reacted to this peptide • 9/12 tested mounted a CTL response to at least one of the six peptides; each of the six peptides elicited a CTL response in at least one individual – this peptide was particularly immunogenic, eliciting a CTL response in five vaccinees • None of the 12 tested had an IgG response to gp120 or gp160 and vaccinees could be differentiated from HIV-1 seropositive individuals with a commercial HIV detection kit – no neutralizing antibodies were observed				
gp160 (298–307)	gp120 (298–307)	RPNNNTRKSI	HIV-1 infection	human (B*07)	Ferris1999, Hammond1995
	• The processing of this epitope is TAP1/2-dependent, as are most Env epitopes, and it contains an N-linked glycosylation site that is glycosylated in Env • Peptide that had been deglycosylated, a process that changes asparagine (N) to aspartic acid (D) (RPNDNTRKSI) was recognized a 100-fold more efficiently than either glycosylated or non-glycosylated RPNNNTRKSI • Position 5 is not involved with HLA B*07 binding, so is probably important for TCR recognition • HIV-1 Env epitopes are typically processed by a TAP1/2 dependent mechanism, which involves cotranslational translocation into the ER, glycosylation, export back into the cytosol, and deglycosylation for processing, and retransport into the ER for the association with class I molecules • The particular pathway of generating an epitope may have an impact on the presentation of that epitope, quantitatively as well as qualitatively				
gp160 (298–307)	gp120 (302–312 HXB2)	RPNNNTRKSI	HIV-1 infection	human (B*0702)	Brander2001
	• C. Brander notes this is a B*0702 epitope				
gp160 (298–307)	gp120 (302–312 HXB2)	RPNNNTRKSI	HIV-1 infection	human (B7)	Safrit1994b
	• CTL from two acute seroconversion cases				
gp160 (298–307)	gp120 (302–312 HXB2)	RPNNNTRKSI	HIV-1 infection	human (B7)	Hammond1995
	• Peptide processed by a TAP-1/2-dependent pathway only • CTL from an acute seroconverter				
gp160 (298–307)	gp120 (302–312 HXB2)	RPNNNTRKSI	HIV-1 infection	human (B7)	Wolinsky1996
	• Longitudinal study of epitope variation in vivo				
gp160 (298–307)	gp120 (302–311 subtype B)	RPNNNTRKSI	HIV-1 infection	human (B7)	Wilson1998b
	• The extent of CTL interclade cross-reactivity from CTL isolated from individuals newly infected with B clade virus was studied, and extensive cross-reactivity was observed • Two HLA B7 individuals had CTL response to B_LAI, A_92UG037 and C_92BR025 gp160, but were B clade strain MN non-responders – the authors note that the B7 epitope RPNNNTRKSI is immunodominant, conserved between the LAI and clade A and C strains, but is very divergent in MN (RPNYNKRKRI), and that this epitope might be dominating the specificity of the response in the HLA B7 individuals				
gp160 (298–307)	gp120 (303–312 SF2)	RPNNNTRKSI	HIV-1 infection	human (B7)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-B7+ individuals that had a CTL response to this epitope broken down by group: 0/4 group 1, 1/3 group 2, and 1/1 group 3				
gp160 (298–307)	gp120 (298–307)	RPNNNTRKSI	HIV-1 infection	human (B7)	Day2001
	• The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person • Subjects with chronic HIV-1 infection recognized between 2-8 out of 11 B7-restricted epitopes • An acute seroconvertor homozygous for the B7 allele recognized five B7-restricted epitopes • The other acute seroconvertor failed to recognize any of the 11 B7-restricted epitopes tested • The B7-restricted CTL response was highly variable and there was no clearly dominant epitope				
gp160 (298–307)	gp120 (298–307)	RPNNNTRKSI	HIV-1 infection	human (B7)	Yu2002a
	• Epitope name: B7-RI10 • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 4/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. 1/4 individuals had detectable responses to this epitope after STI.				
gp160 (298–307)	gp120	RPNNNTRKSI	HIV-1 infection	human (B7)	Appay2002
	• Four HIV patients with prolonged clinically successful anti-viral therapy but with ongoing evidence of replication and Nef mRNA transcription, showed specific T-cell responses by Elispot and Tetramer staining, maintained for 2-4 years after initiation of HAART. • Nef epitope recognition was detected in all 4 subjects, gp120, Pol and Gag-specific in 1 or 2 subjects. • The HIV-specific CD8+ T-cells had an intermediate maturation phenotype characterized by low levels of perforin and high levels of CD27 expression.				
gp160 (298–307)	gp120 (303–312 IIIB)	RPNNNTRKSI	HIV-1 infection	human (B7?)	Wilson1996
	• Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study • RPNNNTRKDI and RPNNNTRKGI, naturally occurring variants, were found in non-transmitting mother – ability to recognize these variants has not yet been determined				
gp160 (299–319)	Env (299–319)	PNNNTRKSIRIGPGQTFYA	HIV-1 infection	human	Novitsky2002
	• HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
gp160 (303–322)	gp120	TRKSIHIGPGRAFYTTGE	Vaccine	murine BALB/c	Luo1998
	Vaccine *Vector/Type:* virus-like particle *Strain:* B subtype consensus *HIV component:* gag, V3				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Intramuscular injection of chimeric gag-env virus-like particles (VLPs) containing V3 loop sequences into BALB/c mice induce V3 specific CTL – TRKSIHIGPGRAFYTTGE is a B subtype consensus that stimulated a cross-reactive CTL response				
gp160 (304–318)	gp120 (304–318 IIIB)	RKSIRIQRGPGRAFV	Vaccine	murine (H-2^d)	Kang1999
	Vaccine *Vector/Type:* virus-like particle *Strain:* HIV-2 VLP, MN, IIIB, RF, SF2 *HIV component:* gag, V3				
	• Virus-like particles could be formed from HIV-2 gag after deleting 143 amino acids at the C-terminal end – a proline rich region in positions 373-377 was critical to VLP formation				
	• CTL responses in BALB/c mice were induced by chimeric gag-V3 particles against the V3 region of HIV-1 clade B isolates IIIB (SIRIQRGRAFVTI), MN (KRIHIGPGRAFYTTK), RF (SITKGPGRVIYATGQ), and SF2 (SIYIGPGRAFHTTGR)				
	• The vaccine induced CTL were cross-reactive with a broad spectrum of B clade isolates, with the exception of the RF V3 which did not induce CTL				
gp160 (306–322)	gp160 (LAI)	SIRIQGPGRAFVTIGI	Vaccine	murine (H-2D^d)	Deml1999
	Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* gp160 *Adjuvant:* CpG oligodeoxynucleotide, alum				
	• Addition of CpG oligodeoxynucleotide to a gp160/alum vaccine given to BALB/c mice shifted the response to Th0/Th1 from Th2, but no still CTL response to this immunodominant epitope was induced				
gp160 (308–321)	Env (IIIB)	RIQRGPGRAFVTIG	Vaccine	murine (Dd)	Ahlers2001
	Vaccine *Vector/Type:* peptide *Strain:* IIIB *HIV component:* V3				
	• Epitope name: P18IIIB				
	• BALB/c and A.AL were immunized with an Env-peptide vaccine construct containing the CTL epitope P18IIIB and the T helper epitope T1, KQIINMWQEVGKAMYA.				
	• Substitution of Glu (wt) to Ala in T1, kqiinmwqAvgkamya, caused increased affinity for MHC class II Ek, resulting in the upregulation of CD40L in the responding Th cells, and shifting the response towards Th1. Increased Th responses stimulated DCs to produce higher levels of IL-12, and B7-1 and B7-2, and enhanced CTL responses to P18.				
	• The modified epitope, T1A, elicited stronger protection against increasing doses of viral challenge with vaccinia expressing HIV-1 IIIB gp120 compared to the wt epitope T1.				
gp160 (308–322)	gp160 (MN)	RIHIGPGRAFYTTKN	Vaccine	human	Pinto1999
	Vaccine *Vector/Type:* peptide *Strain:* MN *HIV component:* V3 *Adjuvant:* Montanide ISA 51				
	• Peptide P18: Eight HIV+ individuals were vaccinated with peptides containing specific T helper, CTL and Ab epitopes in Montanide ISA 51 in a Phase I trial				
	• Four displayed a 4-fold increase in PCLUS 3-18 MN-specific T helper responses				
	• One patient developed a new, sustained P18MN-peptide-specific CTL response – the patient's HLA haplotype was A2,30; B53,7; Cw2,4, and anti-HLA A2 antibody did not inhibit the response, suggesting it was not A2				
	• Patients with low baseline Ab levels developed an increase of neutralizing Ab titers				
	• No significant change was observed in plasma HIV viral loads and CD4 cell counts				
gp160 (308–322)	gp120 (MN)	RIHIGPGRAFYTTKN	HIV-1 infection	chimpanzee	Lubeck1997
	• Epitope-specific CTL detected in chimpanzees immunized with adenovirus-HIV-1 MN gp160 recombinant				
	• CTL response may account for protection against subsequent HIV-1 SF2 challenge in a chimpanzee lacking neutralizing antibodies				
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK	HIV-1 exposed seronegative	human	Pinto1995
	• CTL and T helper cell reactivity in healthcare workers exposed to HIV				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (308–322)	gp120 (313–327 MN)	RIHIGPGRAFYTTKN	HIV-1 exposed seronegative	human	Pinto1995
	• CTL and T helper cell reactivity in healthcare workers exposed to HIV				
gp160 (308–322)	gp120 (110–122)	RIQRGPGRAFVTIGK	Vaccine	murine	Moore2002a
	Vaccine *Vector/Type:* DNA *Strain:* IIIB *Adjuvant:* IL-2, IL-12, IL-15, GMCSF, FLt3 ligand (FL)				
	• Intramuscular immunization of BALB/c mice with DNA vaccines carrying either gp160 or Nef in the expression vector plasmid pNGVL gave different responses – gp160 induced strong gp160-specific CTL and IFN-responses and low-titer humoral responses, and Nef generated humoral (IgG1, IgG2a) responses and IFN-responses but little CTL activity.				
	• Co-injection of DNA plasmids encoding cytokines and/or hematopoietic growth factors, IL2, IL-12, IL-15, Flt3 ligand (FL), and GMCSF tended to give responses that were enhanced quantitatively, but not altered qualitatively.				
	• Co-administration of GMCSF most strongly enhanced CTL and IFN-responses against pNGVL-gp160.				
	• Repeated immunization with pNGVL-Nef failed to induce CTL responses. Co-administration of IL-12 most strongly enhanced humoral and IFNgamma responses.				
	• FL, which enhances innate immune responses, in combination with IL-2, IL-12 or IL-15 generated with most potent Nef responses.				
gp160 (308–322)	Env (315–329)	RIQRGPGRAFVTIGK	Vaccine	murine (A*0201)	Singh2002, Sykes1999
	Vaccine *Vector/Type:* DNA *HIV component:* HIV-1 divided into a 32 plasmids in a ubiquitin expression library				
	• Epitope name: P18				
	• C3H (H-2k) transgenic mice carrying a fused HLA-A*0201 alpha1 and alpha2 and H-2Dk alpha3 hybrid class I molecule were immunized using an epidermal gene gun with an ubiquitin expression library of 32 plasmids that spanned the HIV-1 genome. Ubiquitin targets the expressed HIV-1 peptides to the proteasome.				
	• A single immunization with the UB-HIV-1 library vaccine induced potent, stable and multivalent CTL responses against all library members.				
	• Immunodominant epitopes SLYNTVATL (Gag), ILKEPVHGV(Pol), RIQRGPGRAFVTIGK(P18) and AFHHVAREK (Nef) elicited strong CD8+/IFN-responses and stimulated CTL that were functional in a Cr-release assay and against wild type antigen.				
	• The presence of multiple plasmids HLA-A*0201-restricted CTL epitopes did not decrease CTL immunogenicity, and CTL responses to single peptide immunizations were comparable to responses based on mixtures of either 16 or 32 peptides.				
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK	Vaccine	human (A11)	Achour1994
	Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* gp160				
	• One of 3 HLA type restrictions associated with this peptide				
gp160 (308–322)	gp120 (315–329 BRU)	RIQRGPGRAFVTIGK	HIV-1 infection	human (A2)	Dadaglio1991
	• Defined through blocking CTL activity, and Env deletions				
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK	HIV-1 infection	human (A2)	Clerici1991a
	• Helper and cytotoxic T cells can be stimulated by this peptide (P18)				
gp160 (308–322)	gp120 (308–322 IIIB)	RIQRGPGRAFVTIGK	Vaccine	murine (A2)	Kiszka2002
	Vaccine *Vector/Type:* DNA, DNA with recombinant protein boost *Strain:* IIIB *HIV component:* gp160 *Adjuvant:* IL-12 (IL-12p35 and IL-12p40)				
	• Transgenic mice expressing a HLA-A2/Kb chimeric protein were vaccinated with a full length gp160 or with gp160deltaV3, with the V3 loop deleted. Mice given gp160deltaV3 had a broader immune response than those given gp160, with increased responses to conserved HLA-A2 epitopes in the C1 region of gp120, KLTPLCVTL, and the C-term region of gp41, SLLNATAIAV.				
	• Greater resistance was conferred by the gp160deltaV3 than the gp160 vaccine to a challenge of vaccinia expressing heterologous gp160 from primary isolates (VI-06 and 89.6), and the resistance was conferred by CD8+ T-cells.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The most intense CTL responses to the intact gp160 vaccine were directed at three V3 peptides.				
gp160 (308–322)	gp120 (315–329 IIIB) **Vaccine** *Vector/Type:* vaccinia *HIV component:* gp160 • Two of 3 HLA type restrictions associated with this peptide	RIQRGPGRAFVTIGK	Vaccine	human (A2, A3)	Achour1993
gp160 (308–322)	gp120 (315–329 IIIB) **Vaccine** *Vector/Type:* peptide *Strain:* IIIB *HIV component:* V3 • Positions R(8) and F(10) are important for MHC/peptide interaction.	RIQRGPGRAFVTIGK	Vaccine	murine (D^d)	Takahashi1989a
gp160 (308–322)	gp120 (315–329 IIIB) **Vaccine** *Vector/Type:* peptide *Strain:* IIIB *HIV component:* V3 • Free peptide injected into the footpad of a mouse could stimulate specific CTL	RIQRGPGRAFVTIGK	Vaccine	murine (D^d)	Sastry1992
gp160 (308–322)	gp120 (315–329 IIIB) **Vaccine** *Vector/Type:* peptide *Strain:* MN *HIV component:* V3 • PCLUS 3-18MN synthetic peptide vaccine construct contained T1 helper epitope covalently linked to truncated P18 CTL epitope • A substitution in the T1 peptide stimulated an enhanced Th response and class II binding specificity, which in turn enhanced CTL induction by vaccine • Construct PCLUS 3-18MN is currently in a phase I vaccine clinical trial	RIQRGPGRAFVTIGK	Vaccine	murine (D^d)	Ahlers1997b
gp160 (308–322)	gp120 (313–327 MN) **Vaccine** *Vector/Type:* vaccinia *Strain:* MN, IIIB *HIV component:* gp160 • Y(11 MN) exchange with V(11 IIIB) interchanges specificities	RIHIGPGRAFYTTKN	Vaccine	murine (D^d)	Takahashi1989b
gp160 (308–322)	gp120 (313–327 IIIB, MN, RF) **Vaccine** *Vector/Type:* vaccinia *Strain:* RF *HIV component:* gp160 • Comparison of MN, IIIB, and RF specificities, position 11 is critical	SITKGPGRVIYATGQ	Vaccine	murine (D^d)	Takahashi1992
gp160 (308–322)	gp160 (315–329 IIIB) • Epitope name: P18 • The TCR repertoire and its specificity was studied through analyzing the spectrum of TCR-alpha and beta chains able to reconstitute a reaction to the H-2 Dd-restricted P18 peptide. The RT-1 TCR alpha chain was able to react with 1/3 of the tested TCR beta chains to create a specific response. Experiments in transgenic mice also supported the observation that a single TCR alpha chain would confer the specificity of the response and could interact with a large variety of TCR beta chains.	RIQRGPGRAFVTIGK	in vitro stimulation	murine (Dd)	Yokosuka2002
gp160 (308–322)	gp120 (HXB2) **Vaccine** *Vector/Type:* recombinant protein *HIV component:* Gag, V3 • Gag-V3 fusion protein immunization elicited V3 CTL response in mice	RIQRGPGRAFVTIGK	Vaccine	murine (H-2^d)	Griffiths1993
gp160 (308–322)	gp120 (HXB2) **Vaccine** *Vector/Type:* virus-like particle *HIV component:* Gag, Env • Env bound to virus-like particles (VLPs) can elicit a CTL response that is dependent on the amount of Env presented on the VLP	RIQRGPGRAFVTIGK	Vaccine	murine (H-2^d)	Deml1997
gp160 (308–322)	gp120 (313–327 MN) **Vaccine** *Vector/Type:* DNA *Strain:* MN *HIV component:* gp160, V3	RIHIGPGRAFYTTKN	Vaccine	murine BALB/c (H-2^d)	Fomsgaard1998a

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Enhanced B and CTL responses to the V3 region occur following epidermal immunization by gene gun with a chimeric DNA vaccine of V3-hepatitis B surface antigen relative to a gp160 plasmid vaccine				
gp160 (308–322)	gp120 (313–327 MN)	RIHIGPGRAFYTTKN	Vaccine	murine BALB/c (H-2^d)	Ahlers1996, Ahlers1997a
	Vaccine *Vector/Type:* peptide *Strain:* MN *HIV component:* V3 *Adjuvant:* GMCSF, IL-12 • Vaccine constructs containing helper, antibody and CTL peptide epitopes induce strong Th1, CTL and NAb responses against the autologous HIV-1 virus • The peptide CTL response was as cross-reactive as one elicited by a vaccinia construct expressing rgp160 MN • GM-CSF and IL-12 were the two cytokines most effective for inducing and boosting CTLs				
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK	Vaccine	murine (H-2^d)	Layton1993
	Vaccine *Vector/Type:* virus-like particle *Strain:* IIIB *HIV component:* V3, Gag • V3-Ty-Virus-like particles can induce type-specific CTL in mice in the absence of adjuvant				
gp160 (308–322)	gp120 (IIIB)	RIQRGPGRAFVTIGK	Vaccine	murine (H-2^d)	Barouch1998
	Vaccine *Vector/Type:* DNA *Strain:* IIIB *HIV component:* gp120 *Adjuvant:* IL-2 or IL-2/Ig • A discistronic IL-2 gp120 expression vector gave a weaker CTL response than gp120 alone in the expression vector, however co-administration of an Il-2/IgG fusion protein enhanced the immune response and administration of a Il-2/IgG plasmid had a response that depended on the timing of administration. • This study showed that a response to an HIV-1 DNA vaccine could be either augmented or suppressed by plasmid Cytokine/Ig administration				
gp160 (308–322)	Env (308–322 IIIB)	RIQRGPGRAFVTIGK	Vaccine	murine (H-2^d)	Uno-Furuta2001
	Vaccine *Vector/Type:* peptide *Strain:* IIIB *HIV component:* V3 loop *Adjuvant:* in vivo electroporation, immunostimulatory sequence ISS, B7-1 • Epitope name: P18 • Peptide immunization usually doesn't elicit a good CTL response because epitopes are not internalized and processed and presented, so vaccination with electric pulsing was tried (i.m. injection followed by 8 electric pulses), to enhance peptide uptake through electroporation • BALB/c immunized with HIV P18 or hepatitis C P17 peptides with an electric pulse elicited a CTL response, those that did not receive the pulse did not • The CTL response was enhanced by addition of immunostimulatory sequences ISS in the plasmid pCMV-LacZ, that contains hexamers GACGTC, AGCGCT, AACGCT, sequences common in prokaryotic genomes but rare in eukaryotic genomes that elicit Th1 cytokines and result in B cell and T-cell proliferation • The CTL response was also enhanced by addition of B7-1 cDNA – the B7 family of proteins transduce co-stimulatory signals through interaction with CD28				
gp160 (308–322)	gp160 (MN)	RIHIGPGRAFYTTKN	Vaccine	murine BALB/c and C57/BL6 (H-2^d, H-2^b)	Fomsgaard1998b
	Vaccine *Vector/Type:* DNA *Strain:* MN *HIV component:* gp160 • CTL responses to a primary gene gun vaccination were rapid and strong for several methods of vaccinations: i.m., bupivacaine pretreatment, cardiotoxin pretreatment or gene gun – the CTL response was more rapid and consistent than the antibody response				
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK	Vaccine	murine (H-$2^{d,p,u,q}$)	Shirai1992, Shirai1993
	Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* gp160 • In a murine system multiple class I molecules can present this peptide, called P18, to CTL, including H-2D^d, H-2D^p, H-2D^q, H-2L^q • The MHC class I molecule D^d as well as H-$2^{u,p,q}$, were found to present peptides P18 and HP53 • The V-β usage in T cells showing cross-reaction between these two peptides was conserved for H-$2^{d,u,p}$, but not in H-2^q				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (308–322)	gp160 (IIIB)	GIHIGPGRAFYAARK	Vaccine	murine (H-2D^d)	Morris2000
	Vaccine *Vector/Type:* recombinant protein, peptide *Strain:* IIIB *HIV component:* gp160 *Adjuvant:* mucosal adjuvant LT(R192G)				
	• LT(R192G) induces gp160-specific serum and mucosal IgG1 and IgG2a, systemic CTL activity and Th1 and Th2 cytokine responses upon internasal immunization				
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK	Vaccine	murine (H-2D^d)	Porgador1997
	Vaccine *Vector/Type:* peptide *Strain:* IIIB *HIV component:* V3 *Adjuvant:* cholera toxin adjuvant				
	• A intranasal peptide vaccine with cholera toxin as a mucosal adjuvant was given.				
	• IIIB peptide referred to as R15K				
	• Peptide-specific CTLs were induced after in vitro restimulation with peptide-pulsed targets				
	• R15K was superior at inducing CTL compared to the RGPGRAFVTI, in contrast to the findings of Nehete et al.				
	• Memory CTL responses were induced				
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK	Vaccine	(H-2D^d)	Chiba1999
	Vaccine *Vector/Type:* vaccinia with H1 influenza HA gene cassette *Strain:* IIIB *HIV component:* P18				
	• Vaccine was capable of priming P18IIIB specific CTL in BALB/c mice, but could not induce a P18IIIB-specific antibody response				
gp160 (308–322)	gp120 (multiple)	RIHIGPGRAFYTTKN	Vaccine	murine (H-2D^d)	Casement1995
	Vaccine *Vector/Type:* peptide *Strain:* MN, SC *HIV component:* V3				
	• V3 peptides from MN and SC induce murine CTL that are cross-reactive with diverse strains				
gp160 (308–322)	gp120 (313–327 MN)	RIHIGPGRAFYTTKN	Vaccine	murine (H-2D^d)	Newman1997
	Vaccine *Vector/Type:* recombinant protein *Strain:* MN *HIV component:* gp120 *Adjuvant:* QS-21 adjuvant				
	• MN vaccine induced CTL reactive with MN, IIIB and RF vaccinia-expressed Env, but not this peptide				
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK	Vaccine	murine (H-2D^d)	Newman1997
	Vaccine *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* gp120 *Adjuvant:* QS-21 adjuvant				
	• IIIB vaccine induced IIIB type-specific CTL to this peptide (P18), and an additional Env CTL response that was cross-reactive				
gp160 (308–322)	gp120 (315–329)	RIQRGPGRAFVTIGK	Vaccine	murine (H-2D^d)	Takahashi1988
	Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* gp160				
	• V3 loop CTL response in mice vaccinated with gp160				
gp160 (308–322)	gp120 (315–329)	RIQRGPGRAFVTIGK	Vaccine	murine BALB/c (H-2D^d)	Fukasawa1998
	Vaccine *Vector/Type:* liposome *Strain:* IIIB *HIV component:* V3 *Adjuvant:* oligomannose				
	• The peptide RIQRGPGRAFVTIGK was incorporated into liposomes and given as a subcutaneous injection, which induces a MHC class I restricted CTL response in mice				
	• Liposomes coated with oligomannose show no toxicity and can elicit a potent CTL response upon a single subcutaneous infection, while non-coated liposomes do not, suggesting that oligomannose may be a good adjuvant for CTL responses				
gp160 (308–322)		RIQRGPGRAFVTIGK	Vaccine	murine (H-2D^d)	Lu2000a
	Vaccine *Vector/Type:* fusion protein with anthrax delivery domain *HIV component:* V3 *Adjuvant:* B. anthracia lethal toxin LF component				
	• Epitope name: P18				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Bacillus anthrax lethal toxin (LFn)-HIV fusion proteins are candidate HIV vaccines that are safe in mice, and LFn-V3 region fusion proteins induce CD8 T cells in BALBc mice. LFn causes exogenous protein to be taken up and processed in a class I pathway. Expressed proteins from Gag p24 and nef fragments cloned into the LFn expression plasmid stimulate gag-specific CD4 proliferation and CTL responses in HIV-infected donor PBMCs in vitro.				
gp160 (308–322)	gp120 (V3) (MN)	RIHIGPGRAFYTTKN	Vaccine	murine (H-2D^{d})	Staats2001
	Vaccine *Vector/Type:* peptide *Strain:* IIIB *HIV component:* V3 *Adjuvant:* cholera toxin (CT), IL-1alpha, IL-12, IL-18, GM-CSF				
	• Cholera toxin (CT) is a potent adjuvant used in animal studies that is not safe in humans, so combinations of cytokins were used in nasal immunization of BALB/c mice V3 peptides to attempt to replace CT as a potent adjuvant.				
	• Peptide vaccine induced CTL activity was significantly increased by IL-1alpha , IL-18, and GMCSF given alone as adjuvant, but CT gave more potent CTL activity than any single cytokine.				
	• Combinations of cytokins could be more potent that CT as an adjuvant. The highest tetramer binding of H-2Dd peptide-specific PBMC after nasal immunization was observed with IL-1alpha plus IL-18 as adjuvant.				
	• Nasal immunization with HIV peptide in the presence of IL-1alpha, IL-12 and GM- CSF induced IFN-gamma-secreting cells in the cervical lymph node, the lung and the spleen, and was associated with upregulation of MHC class II and B7.1 on nonlymphocytes in NALT/nasal mucosal cells.				
	• Consistent results were obtained for the IIIB and the MN peptides.				
gp160 (308–322)	gp160 (315–329 MN)	RIHIGPGRAFYTTKN	in vitro stimulation	murine (H-2D^{d})	Yokosuka2002
	• Epitope name: P18				
	• The TCR repertoire and its specificity was studied through analyzing the spectrum of TCR-alpha and beta chains able to reconstitute a reaction to the H-2 Dd-restricted P18 peptide. The RT-1 TCR alpha chain was able to react with 1/3 of the tested TCR beta chains to create a specific response. Experiments in transgenic mice also supported the observation that a single TCR alpha chain would confer the specificity of the response and could interact with a large variety of TCR beta chains.				
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK	Vaccine	murine (H-2D^{d,p,q}, H-2^{u})	Shirai1996b
	Vaccine *Vector/Type:* vaccinia *HIV component:* gp160				
	• Multiple murine MHC can cross-present this epitope (P18) and HP53, DRVIEVVQGAYRAIR, to specific CTL				
gp160 (309–317)	gp120 (310–318 SF2)	IYIGPGRAF	HIV-1 infection	human (A*2402)	Ikeda-Moore1997
	• Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402				
	• This peptide induced CTL in 1/4 HIV-1+ people tested				
	• IYIGPGRAF bound to A*2402 strongly, the epitope can be processed in a vaccinia construct and presented – no specific CTL clones were obtained				
gp160 (309–318)	gp120 (314–323 CM243 subtype CRF01)	ITVGPGQVFY	HIV-1 infection	human (A11)	Sriwanthana2001
	• Epitope name: E309-318				
	• This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand				
	• HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed				
	• This epitope was strongly reactive in HIV+ control study subject 184 who carried HLA-A11				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (309–318)	gp120 (314–323 CM243 subtype CRF01)	ITVGPGQVFY	HIV-1 infection	human (A11)	Bond2001
	• HLA-A11 CRF01 (called subtype E in Bond et al.) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive • 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 finding and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified • This is one of the new A11 epitopes identified through the streamlined EpiMatrix method, and 2/8 tested FSWs recognized it • This epitope was not conserved in other subtypes, and exact matches were rare				
gp160 (310–318)		HIGPGRAFY	HIV-1 infection	human (A*3002)	Sabbaj2002b
	• Epitope name: Env-HY9 • This study monitored epitope responses in HIV-1 infected minority women living in the United States • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release • This epitope was newly defined in this study • Subject 00RCH33 was on HAART had a viral load of 2900 and CD4 count of 727 and also recognized the epitopes YPLTFGWCY, Nef(135-143), HLA B*5301; AETFYVDGA, RT(437-445), HLA B*4501; and RSLYNTVATLY, p17(76-86), HLA A*3002 • Among HIV+ individuals who carried HLA A30, 3/16 (19%) recognized this epitope				
gp160 (310–318)		HIGPGRAFY	HIV-1 infection	human (A02)	Sabbaj2002b
	• Epitope name: Env-HY9 • Among HIV+ individuals who carried HLA A02, 6/29 (21%) recognized this epitope				
gp160 (310–323)	gp120 (315–328 MN)	HIGPGRAFYTTKNI	Vaccine	murine (H-2D^d)	Arp1999
	Vaccine *Vector/Type:* canarypox prime with pseudovirion boost *Strain:* MN, IIIB *HIV component:* gp120, Gag, Pro • Epitope name: p97 • The vaccine vCP205, canarypox vector, MN gp120 + Gag/Pro IIIB, with a HIV-1 pseudovirion boost was given to mice;) • HIV-1 pseudovirion boost enhanced the CTL to this epitope in immunized BALB/ c mice as measured by CTL lysis and IFN gamma production				
gp160 (311–318)	(MN)	IGPGRAFY	Vaccine	murine (H-2D^d)	Golding2002a
	Vaccine *Vector/Type:* B. abortus-peptide conjugate *Strain:* MN *HIV component:* V3 • Intranasal immunization of B. abortus conjugated to V3 peptides induces mucosal IFN-gamma producing T-cell responses in BALB/c mice				
gp160 (311–319)	gp120 (311–320 IIIB)	RGPGRAFVT	Vaccine	murine (A2)	Kiszka2002
	Vaccine *Vector/Type:* DNA, DNA with recombinant protein boost *Strain:* IIIB *HIV component:* gp160 *Adjuvant:* IL-12 (IL-12p35 and IL-12p40) • Transgenic mice expressing a HLA-A2/Kb chimeric protein were vaccinated with a full length gp160 or with gp160deltaV3, with the V3 loop deleted. Mice given gp160deltaV3 had a broader immune response than those given gp160, with increased responses to conserved HLA-A2 epitopes in the C1 region of gp120, KLTPLCVTL, and the C-term region of gp41, SLLNATAIAV. • Greater resistance was conferred by the gp160deltaV3 than the gp160 vaccine to a challenge of vaccinia expressing heterologous gp160 from primary isolates (VI-06 and 89.6), and the resistance was conferred by CD8+ T-cells. • The most intense CTL responses to the intact gp160 vaccine were directed at three V3 peptides.				
gp160 (311–319)	gp120 (312–320 SF2)	IGPGRAFHT	Vaccine	murine (D^d)	Selby1997
	Vaccine *Vector/Type:* DNA *Strain:* SF2 *HIV component:* gp120				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Murine CTL response to peptide observed after immunization with DNA plasmid containing HIV-1 (SF2) gp120 gene regulated by bacteriophage T7 promoter • CTL response required coadministration of rec vaccinia virus expressing T7 RNA polymerase or T7 RNA polymerase soluble protein				
gp160 (311–319)	gp120 (SF2)	IGPGRAFHT	Vaccine	murine (H-2D^d)	Barnett1997
	Vaccine *Vector/Type:* DNA prime with rgp120 boost *Strain:* SF2 *HIV component:* gp120 • CTL were induced by vaccine, and restimulated in vitro with V3 peptide • DNA vaccine with protein boost stimulated both CTL and antibodies • Strains SF2 (IGPGRAFHT), US4 (IGPGRAFYA), and CM235 (IGPGQVFYR) were tested				
gp160 (311–320)	gp160 (318–327 IIIB)	RGPGRAFVTI	Vaccine	Macaca fuscata	Okuda1997
	Vaccine *Vector/Type:* DNA prime with peptide boost *Strain:* IIIB *HIV component:* gp160, V3, CD4BS, HPG30 • Murine BALB/c (H-2^d) and macaque both showed highest level of CTL vaccine response when a DNA vaccine was boosted with a peptide including four peptide subtypes of the V3 region, HPG-30 and a fragment of the CD4 binding region				
gp160 (311–320)	gp120 (318–327)	RGPGRAFVTI	HIV-1 infection	human	Kmieciak1998b
	• Increased CTL response to cells expressing a VV construct ΔV3 mutant compared with a full-length env gene product • This epitope doesn't have A2 anchors, but has features that confer promiscuous A2 binding, which may relate to the inhibitory effect seen in this paper				
gp160 (311–320)	Env (IIIB)	RGPGRAFVTI	Vaccine	murine BALB/c	Lu1999
	Vaccine *Vector/Type:* DNA *Strain:* IIIB *HIV component:* gp160, rev *Adjuvant:* MIP-1alpha • MIP-1alpha co-inoculation increased IgG1/IgG2a ratio T-helper type 1 response. • A MIP-1 alpha expression plasmid increased the CTL response to this DNA vaccine, as well as the T help response, presumably by the MIP-1 alpha interacting with T lymphocytes and macrophages				
gp160 (311–320)		RGPGRAFVTI	Vaccine	murine	Barouch2002
	Vaccine *Vector/Type:* DNA *Strain:* BH10 *HIV component:* gp120 *Adjuvant:* GMCSF (bicistronic) • Epitope name: P18 • gp120 encoding DNA co-injected with a plasmid carrying GMCSF gave meager CD4+ T-cell responses in BALB/c mice relative to the enhanced response to bicistronic gp120 and GMCSF cloned into the same vector and expressed from the same promoter. • Both mono and bicistronic DNA vaccines induced similar CTL responses directed against the H-2Dd restricted P18 peptide RGPGRAFTVTI in murine splenocytes despite the greatly enhanced proliferative responses.				
gp160 (311–320)	gp120 (313–322 BRU)	RGPGRAFVTI	Vaccine	murine	Arora2001
	Vaccine *Vector/Type:* DNA *Strain:* BRU *HIV component:* gp160, tat, rev • Epitope name: Pep 09 • Plasmid DNA encoding gp160, tat, rev was given i.m. to immunize BALB/c mice. • Vaccine-induced CTL activity produced a low degree of cell lysis of V3-peptide pulsed target cells, using a B (RGPGRAFVTI) or C (RIGGPGQTFYATG) clade V3 peptides. Th1 proliferative T-cell responses were observed, and weak Ab responses.				
gp160 (311–320)	gp160 (318–327 IIIB)	RGPGRAFVTI	in vitro stimulation	human (A*0201)	Alexander-Miller1996
	• This eptiope stimulates a CTL line derived from an HIV negative donor. • This immunogenic peptide does not have the known binding motif for A2.1 • The same optimal peptide for this human HLA-A2.1 epitope was observed for a murine H-2 D^d epitope				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (311–320)	gp120 (311–320 IIIB)	RGPGRAFVTI		human (A*0201)	Brander2001
	• C. Brander notes this is an A*0201 epitope				
gp160 (311–320)	gp160 (318–327 IIIB)	RGPGRAFVTI	Vaccine	human (A2)	Achour1996
	Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* gp160				
	• Individual was immunized with rec vaccinia gp160 IIIB and boosted with purified gp160				
	• Lysis only occurs with IIIB P18 peptide pulsed onto autologous targets; MN, RF, SIMI P18 peptides fail to stimulate CTL				
	• Restimulating immune cells from gp160 IIIB vaccinees with MN, RF, or SIMI P18 did not enhance the MN, RF, or SIMI specific CTL response				
gp160 (311–320)	gp160 (318–327 SIMI)	MGPKRAFYAT	Vaccine	human (A2)	Achour1996
	Vaccine *Vector/Type:* vaccinia prime with rgp160 boost *Strain:* SIMI *HIV component:* gp160				
	• Individual was immunized with rec vaccinia gp160 SIMI and boosted with purified recombinant gp160 SIMI				
	• P18 MN and RF peptides were able to stimulate the HIV-specific CTL that arose in response to the SIMI vaccination, thus the P18 MN peptide (IGPGRAFYTT) and the P18 RF peptide (KGPGRVIYAT) could cross-react				
	• The P18 IIIB peptide does not cross-react (RGPGRAFVTI in the epitope region)				
	• gp160 SIMI primed immune cells could generate a significantly broader specificity when stimulated with P18 MN or P18RF peptides, but not P18 IIIB				
gp160 (311–320)	gp120 (311–320)	RGPGRAFVTI	HIV-1 infection	human (A2)	Day2001
	• The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)				
	• 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person				
gp160 (311–320)	gp160 (318–327 IIIB)	RGPGRAFVTI	Vaccine	murine (A2.1)	Peter2001
	Vaccine *Vector/Type:* peptide *Strain:* LAI *Adjuvant:* P30, incomplete Freund's adjuvant (IFA), Montanide (ISA 720), PLG-microsphere				
	• Epitope name: LR25				
	• The stability of peptide binding to HLA-A2.1 was determined for six HLA-A2.1 peptides included in this vaccine study – ILKEPVHGV (RT), SLYNTVATL (p17), SLLNATDIAV (gp41) and LLWKGEGAV (RT) all bound with high affinity comparable to a influenza epitope reference (GILGFVFTL), while RGPGRAFVTI and VIYQYMDDL bound with a lower affinity (relative binding activity = 0.01).				
	• The four high-affinity peptides formed stable complexes with half-lives ranging between 8 and 32 hours, while the low affinity peptides had half lives of less than an hour.				
	• HLA-A2.1 transgenic mice were immunized with the six HIV-1 peptides and P30, as a universal T-helper epitope, with IFA or Montanide or microspheres as adjuvants.				
	• All peptides except VIYQYMDDL induced a stong CTL response in Cr-release assays - stronger responses were observed when peptides were delivered alone, indicating immunodominance when the combination was used.				
gp160 (311–320)	gp160 (318–327 IIIB)	RGPGRAFVTI	Vaccine	murine (D)	Nehete1995
	Vaccine *Vector/Type:* peptide *Strain:* IIIB *HIV component:* V3				
	• RGPGRAFVTI was defined as the optimal peptide for vaccination, out of RIQRGPGRAFVTIGK				
	• This peptide, in a carrier-free form in Freund's adjuvant, could stimulate Env specific CTL in BALB/c mice				
gp160 (311–320)	gp160 (318–327 IIIB)	RGPGRAFVTI	Vaccine	murine (D^d)	Takahashi1993
	Vaccine *Vector/Type:* peptide *Strain:* IIIB *HIV component:* V3				
	• Successful priming with vaccination of peptide pulsed splenic dendritic cells				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (311–320)	gp160 (318–327 IIIB)	RGPGRAFVTI	Vaccine	murine (D^d)	Takahashi1996
	Vaccine *Vector/Type:* peptide *Strain:* IIIB *HIV component:* V3				
	• Exposure of CD8+ CTL to free peptide corresponding to the epitope results in strong inhibition of the CTL response to targets presensitized with the same peptide				
	• The authors propose this is due to a "self-veto", where the CTL is inactivated by a CD8+ cell carrying the appropriate peptide-MHC complex				
gp160 (311–320)	gp160	RGPGRAFVTI	Vaccine	murine (H-2^d)	Gherardi2000
	Vaccine *Vector/Type:* DNA, vaccinia *HIV component:* env *Adjuvant:* IL-12				
	• Induction of HIV-1 specific CD8 gamma IFN secreting cells was enhanced when IL-12 and Env were given together in a prime, followed by a VV expressing Env boost				
	• If IL-12 was also delivered as a boost from the viral vector, impairment of the IL-12 effects was noted, indicating that the vaccination schedule can be a critical parameter for success with DNA and vaccinia vectors used in combination with immunomodulators				
	• The negative effect observed when IL-12 was delivered with the boost involved nitric oxide				
gp160 (311–320)	Env	RGPGRAFVTI	Vaccine	murine (H-2^d)	Xin1999
	Vaccine *Vector/Type:* DNA *Strain:* IIIB *HIV component:* gp160, rev *Adjuvant:* IL-15 and IL-2, IL-12				
	• A study of the DNA vaccine pCMV160IIIB/REV with IL-15 and IL-2 or IL-12 expression plasmids.				
	• Intranasal immunization of BALB/c mice with HIV DNA and IL-15 plasmid induced increased Th1 and CTL responses				
	• Co-administration of IL-15 with IL-12 or IL-2 plasmids did not alter the effect of IL-15				
	• Both the CTL (peptide pulsed targets) and DTH response (injection of peptide into footpad) to this peptide was monitored				
	• The Ab response to NNTRKSIRIQRGPGRAFVTIGKIGN was monitored, and IL-15 co-administration resulted in a decrease in the IgG1/IgG2a ratio				
gp160 (311–320)	Env	RGPGRAFVTI	Vaccine	murine (H-2^d)	Villacres1999
	Vaccine *Vector/Type:* vaccinia, Sindbis *HIV component:* V3				
	• HIV-1 epitope p18 was expressed in two different vaccine vectors and the CTL response was compared in BALB/c mice				
	• Class I tetramer staining showed that up to 13% of the CD8+ splenocytes were p18 specific in the acute response using vaccinia, only 4% using Sindbis				
	• vp18 had more gamma IFN secreting splenocytes and activated CD4+ and CD8+ T cells				
	• The overall decline in CD8+ T cells in the transition into memory was 2-3 fold for both vectors				
	• Sindbis virus recombinants induced protective memory cytotoxic T cells, although reduced quantitatively, without vaccinia associated inflamation and replication				
gp160 (311–320)	Env (318–327)	RGPGRAFVTI		murine (H-2^d)	Lopez2000
	• A series of protease and proteasome inhibitors was used to identify elements of the processing pathway of this epitope, called p18, both from within Env and from within a chimeric hepatitis B protein which allows proper processing				
	• Lactacystin, a proteasome inhibitor, partially inhibits endogenous processing of p18 epitope suggesting both a proteasome pathway and an additional pathway can be used				
	• Both TAP dependent and TAP-independent pathways can be used				
	• 1,10-phenanthrolin (metallopeptidases inhibitor) blocks epitope presentation demonstrating metalloproteinase processing in the Tap-dependent pathway				
	• The Tap-independent pathway does not involve processing by metalloproteinases				
	• This epitope is immunodominant in mice, and is presented by multiple human HLA alleles – it as been suggested that the high processing efficiency of this epitope might result in poor presentation of co-expressed epitopes				
gp160 (311–320)	gp120	RGPGRAFVTI	Vaccine	murine (H-2^d)	Hanke1998a, Hanke1998b
	Vaccine *Vector/Type:* vaccinia *HIV component:* polyepitope				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This murine epitope was incorporated into a vaccine of CTL epitopes expressed together including 20 HIV epitopes recognized by humans from 12 HLA types, one murine HIV epitope and three macaque HIV epitopes, delivered in a vaccinia virus Ankara (VVA) construct • The murine vaccination was more effective at generating CTL when given i.v. rather than i.m.				
gp160 (311–320)	gp160 (318–327 IIIB)	RGPGRAFVTI	Vaccine	murine BALB/c (H-2^d)	Hamajima1997
	Vaccine *Vector/Type:* peptide *HIV component:* V3, HPG30, CD4BS *Adjuvant:* IL-12 • B cell epitope HGP-30 also serves as a CTL epitope • Vaccine combined HGP-30, V3 loop peptide variants, and CD4 binding site peptide • IL-12 expression plasmid included with the vaccination enhanced the CTL response				
gp160 (311–320)	gp160 (318–327 IIIB)	RGPGRAFVTI	Vaccine	murine (H-2^d)	Arai2000
	Vaccine *Vector/Type:* DNA *Strain:* IIIB *HIV component:* gp160 *Adjuvant:* 8 Br-cAMP/CMV promotor • Low-dosage 8 Br-cAMP given in combination with a DNA vaccine to BALB/c mice increased IgG and sIgA levels, and enhanced Th1, Th2 and CTL activity – the adjuvant activity may be mediated by activation of the CMV promotor in the DNA vaccine				
gp160 (311–320)	gp120 (318–327 IIIB)	RGPGRAFVTI	Vaccine	murine (H-2^d)	Goletz1997
	Vaccine *Vector/Type:* fusion protein with anthrax delivery domain *HIV component:* gp120 • Anthrax lethal toxin can deliver proteins to the cytosol of eukaryotic cells • A fusion protein linking the delivery domain of the anthrax protein to gp120 achieved cellular uptake, and gp120 was processed allowing presentation of this V3 epitope to CTL in vitro				
gp160 (311–320)	gp160 (318–327 IIIB)	RGPGRAFVTI	in vitro stimulation	murine (H-2^d)	Takahashi2001
	• Epitope name: I-10 • Pre-incubation of HIV-1 (IIIB) gp160 specific CTL with peptide without APCs reduced cytolytic activity 3.5 fold and induced peptide concentration dependent IL-2 unresponsiveness that might be due to IL-2Rbeta down regulation • An enhanced cytolytic activity was observed by addition of anti-IFN-gamma, TNF-alpha or MIP-1beta to I-10 suppressed CTLs				
gp160 (311–320)	gp160 (IIIB)	RGPGRAFVTI	Vaccine	murine (H-2^d)	Shirai2001
	Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* gp160 • Helicobacter pylori induces Th1 responses early, but predominantly Th2 responses later in infection (at 6 weeks) – differentiation of HIV-1 gp160 CD4+ help and CD8+ CTL effector cells in response to HIV gp160-vaccinia vaccination is impaired in BALB/c mice infected with H. pylori				
gp160 (311–320)	gp120 (318–327 IIIB)	RGPGRAFVTI	Vaccine	murine (H-$2^{d,p,u}$)	Shirai1997
	Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* gp160 • Three class I MHC, H-$2^{d,p,u}$, that differ in sequence and serology, cross-present this peptide to T cells of each of the other haplotypes • The amino acids R, F, and I are each critical for strong CTL activity with all three MHC molecules				
gp160 (311–320)	gp160	RGPGRAFVTI	Vaccine	murine (H-2^{d17})	Hanke1998a
	Vaccine *Vector/Type:* vaccinia *HIV component:* polyepitope • MVA is an attenuated vaccinia that can not replicate in mammalian cells – strings of CTL epitopes were delivered and expressed in a MVA DNA vector • γ IFN and CTL activity were induced after a single vaccination • An MVA boost enhanced the response				
gp160 (311–320)	Env (89.6)	IGPGRARYAR	Vaccine	murine BALB/c (H-2D)	Belyakov1998b
	Vaccine *Vector/Type:* vaccinia *Strain:* 89.6 *HIV component:* gp160				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Recombinant modified vaccinia virus Ankara (MVA), an attenuated vaccina which has lost the ability to replicate in mammalian cells, was used as the live vector for this vaccine study • A single intrarectal mucosal immunization resulted in long lasting mucosal CTL responses and production of proinflammatory cytokines in mucosal sites, indicating that MVA was as effective in inducing mucosal CTL as replicating recombinant vaccinia				
gp160 (311–320)	Env (IIIB)	IGPGRARYAR	Vaccine	murine BALB/c (H-2D)	Belyakov1998a
	Vaccine *Vector/Type:* peptide *Strain:* IIIB *HIV component:* V3 • HIV protection and mucosal CTL response was studied – an HIV peptide immunogen could protect against gp160 expressing vaccinia in a murine intrarectal challenge system in which neutralizing Abs did not play a role, demonstrating mucosal CTL at the site of exposure can be protective				
gp160 (311–320)	gp120 (MN)	IGPGRAFYTT	Vaccine	murine (H-2D^d)	Lapham1996
	Vaccine *Vector/Type:* B. abortus-peptide conjugate • B. abortus-peptide conjugate induced a virus-specific CTL response in CD4+ lymphocyte depleted mice				
gp160 (311–320)	gp160 (IIIB)	RGPGRAFVTI	Vaccine	murine (H-2D^d)	Bruce1999
	Vaccine *Vector/Type:* non-replicating adenovirus *Strain:* IIIB *HIV component:* Env, Rev • A good HIV-1 Env immune response using non-replicating adenovirus vectors in BALB/c mice is dependent upon the presence of the stimulatory tat/rev 5'splice-donor site sequence and the presence of Rev • Administration of monocistronic RAd501 expressing env and RAd46 expressing rev resulted in a positive CTL response, but required two immunizations for a CTL response comparable to that induced by the bicistronic virus RAd142 • Administration of RAd501 alone gave a low CTL response, but no humoral response, suggesting a lower level of antigen may be required to stimulate CTL				
gp160 (311–320)	gp120 (MN)	IGPGRAFYTT	Vaccine	murine (H-2D^d)	Lapham1996
	Vaccine *Vector/Type:* B. abortus-peptide conjugate • B. abortus-peptide conjugate induced a virus-specific CTL response in CD4+ lymphocyte depleted mice				
gp160 (311–320)	gp160 (318–327 IIIB)	RGPGRAFVTI	Peptide-HLA interaction	murine (H-2D^d)	Takeshita1995
	• XGPXRXXXXI are critical for binding, consistent with H-2D^d motif XGPX(RKH)XXX(X)(LIF)				
gp160 (311–320)	Env	RGPGRAFTVTI	Vaccine	murine (H-2D^d)	Hanke1999a, Hanke1999b
	Vaccine *Vector/Type:* DNA *HIV component:* V3 • Vaccinated mice elicited a CTL response to a gene gun-delivered multiepitope vaccine to two epitopes studied that are known to elicit CTL in mice: SYIPSAEKI from Plasmodium berghei and RGPGRAFTVTI from HIV-1 Env • Different vaccination protocols were tested and it was found that a gene gun mediated delivery followed by an MVA boost was as good as i. m. immunization followed by a MVA boost – this is advantageous as gene gun delivery requires far less DNA than i.m. DNA priming • CTL activity was high (60% - 70% specific lysis at effector target) when vaccinated with a single gene gun immunization and an MVA boost, and improved with two gene gun vaccinations				
gp160 (311–320)	Env (IIIB)	RGPGRAFVTI	in vitro stimulation	murine (H-2D^d)	Nakagawa2000
	• Epitope name: I-10 • The CTL line LINE-IIIB was generated by repetitive restimulation of BALB/c spleen cells with vSC-25, IIIB gp160-expressing vaccinia • RGPGRAFVTI represents the active minimal epitope within the previously described immunodominant epitope P18IIIB (RIQRGPGRAFVTIGK, gp160(308-322)				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• External processing of P18IIIB results in the removal of the 2 C-terminal residues (GK) of I-10 by ACE (angiotensin-1-converting-enzyme) in sera to produce I-10, and this processing is essential for target cell presentation of RIQRGPGRAFVTIGK				
gp160 (311–320)	Env (IIIB)	RGPGRAFVTI	Vaccine	murine (H-2D^d)	Haglund2002a
	Vaccine *Vector/Type:* vesicular stomatitis virus (VSV), vaccinia *Strain:* Env, IIIB; Gag HXB2 *HIV component:* Gag, Env • Epitope name: p18-I10 • BALB/c mice were vaccinated with rec vesicular stomatitis virus (rVSV) expressing either HIV-1 Gag, Env, or both, and compared to using rec Env and Gag in vaccinia virus (rVVs). The primary response was determined by cell lysis, cytokine production and tetramer staining. • Primary CTL responses to the immunodominant Env (RGPGRAFVTI) epitope peaked 5-7 days after intraperitoneal vaccination with Env-rVSV, 40% of the CD8+ cells were tetramer positive, and this response was 6-fold higher than the response to Env-rVV. • Vaccinating with GagEnv-rVSV carrying both Gag and Env allowed recognition of both HIV-1 proteins, but at reduced levels compared to either Gag-rVSV or Env-rVSV alone. • Intranasal immunization with Env-rVSV yielded CTL responses that were strong but reduced compared to an intraperitoneal route.				
gp160 (311–320)	Env (IIIB)	RGPGRAFVTI	Vaccine	murine (H-2D^d)	Haglund2002b
	Vaccine *Vector/Type:* vesicular stomatitis virus (VSV), vaccinia *Strain:* Env, IIIB; Gag, HXB2 *HIV component:* Gag, Env • Epitope name: p18-I10 • BALB/c mice were vaccinated with rec vesicular stomatitis virus (rVSV) expressing either HIV-1 Gag or Env, or both, and retention of memory responses and recall responses were studied by tetramer staining and IFN-gamma production. • Seven months after vaccination with Env-rVSV, 6% of the CD8+ cells were tetramer positive for the immunodominant Env epitope; these cells had a memory phenotype, CD44-Hi positive. • Env in rec vaccinia virus (Env-rVV) elicited a strong recall response, with up to 45% to the CD8+ T-cell population tetramer positive and activated (expressing CD62L-Lo), and capable of IFN-gamma production. • A prime with Env-rVSV and heterologous boost of Env-rVV gave remarkably high levels of memory cells, with approximately 1/3 of the CD8+ splenocytes being Env specific memory cells 150 days after the boost. • A Gag-rVSV or EnvGag-rVSV prime and with a heterologous Gag-rVV or EnvGag-rVV boost combination gave 40% tetramer positive CD8+ cells, but the fraction of IFN-gamma producing cells was only about 25%. Still the heterologous vector prime-boost combination showed a profound benefit. • A HIV-1 protein rVSV prime, rVV boost was a more potent combination than a vector reversal of a rVV prime and rVSV boost.				
gp160 (311–320)	gp120 (V3) (IIIB)	RGPGRAFVTI	Vaccine	murine (H-2D^d)	Staats2001
	Vaccine *Vector/Type:* peptide *Strain:* IIIB *HIV component:* V3 *Adjuvant:* cholera toxin (CT), IL-1alpha, IL-12, IL-18, GM-CSF • Cholera toxin (CT) is a potent adjuvant used in animal studies that is not safe in humans, so combinations of cytokins were used in nasal immunization of BALB/c mice V3 peptides to attempt to replace CT as a potent adjuvant. • Peptide vaccine induced CTL activity was significantly increased by IL-1alpha , IL-18, and GMCSF given alone as adjuvant, but CT gave more potent CTL activity than any single cytokine. • Combinations of cytokins could be more potent that CT as an adjuvant. The highest tetramer binding of H-2Dd peptide-specific PBMC after nasal immunization was observed with IL-1alpha plus IL-18 as adjuvant. • Nasal immunization with HIV peptide in the presence of IL-1alpha, IL-12 and GM- CSF induced IFN-gamma-secreting cells in the cervical lymph node, the lung and the spleen, and was associated with upregulation of MHC class II and B7.1 on nonlymphocytes in NALT/nasal mucosal cells. • Consistent results were obtained for the IIIB and the MN peptides.				
gp160 (311–320)	gp160 (318–327 IIIB)	RGPGRAFVTI	Vaccine	murine (H-2D^d)	Wierzbicki2002
	Vaccine *Vector/Type:* DNA prime with vaccinia boost *Strain:* IIIB *HIV component:* gp160 *Adjuvant:* PLG-microparticle, liposome, beta-glucan lentinan, IL-2/Ig				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• BALB/c mice were give an oral immunization with (PLG)-encapsulated plasmid DNA expressing gp160 and a boost of rec gp160 vaccinia vectors (rVV) with addition of murine IL-2/Ig plasmid or lentinan-associated liposomes. Lentinan increased CTL activity as measured by Cr-release assays against the immunodominant epitope RGPGRAFVTI, but didn't alter Ab responses. IL-2/Ig increased both type I and II activities, and increased Env specific CTL and Abs. Administration of liposomes and PLG microparticles with adjuvants facilitated gastrointestinal uptake.				
gp160 (311–320)	gp120 (LAI)	RGPGRAFVTI	Vaccine	murine (H-2D^d)	Horner2001
	Vaccine *Vector/Type:* protein *Strain:* LAI *HIV component:* gp120 and Pr55gag *Adjuvant:* immunostimulatory sequence (ISS), CpG • Epitope name: P18 • Immunostimulatory sequences (ISS), also known as CpG motifs, stimulate innate immunity and enhance vaccine-specific immune responses. • Intranasal immunization (i.n.) of BALB/c mice was more effective than intradermal (i.d.), and immunization with a gp120-ISS conjugate was more potent than immunizing with gp120 and separate ISS molecule – increased IgG1, IgG2a, IFN-gamma, MIP1-alpha and MIP1-beta production was observed, and only i.n. immunization gave IgA responses. • The highest mucosal CTL activity in both the Lamina Propria and the Peyer's Patch was observed following intranasal delivery with the gp120/ISS conjugate. • Cytokine, chemokine and CTL responses following gp120/ISS conjugate vaccination were CD4+ T-cell independent; gp120 specific antibodies were dependent on helper T cells.				
gp160 (311–320)	gp160 (V3) (IIIB)	RGPGRAFVTI	Vaccine	murine (H-2D^d)	Takahashi2002
	Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* gp160 • Epitope name: I10 • During acute infection, high doses of virus result in "clonal exhaustion", a depletion of antigen specific T-cells. • Recently stimulated CTL from BALB/c mice vaccinated with gp160-vaccinia showed a dose- and time-dependent induction of apoptosis when stimulated with antigenic peptide or H-2Dd/peptide tetramers. • Restimulated CTL showed an upregulation of CD3-chain phosphorylation in comparison to cells stimulated with target cells, indicative of TCR-mediated apoptosis. Furthermore, apoptosis was inhibited by cyclosporin A and U0126, a mitogen activated kinase inhibitor specific for the ERK1/ERK2 MAPK kinase pathway, and a caspase 3 inhibitor.				
gp160 (311–320)	gp160 (V3) (MN)	IGPGRAFYAT	Vaccine	murine (H-2D^d)	Takahashi2002
	Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* gp160 • Epitope name: MNT10 • During acute infection, high doses of virus result in "clonal exhaustion", a depletion of antigen specific T-cells. • Recently stimulated CTL from BALB/c mice vaccinated with gp160-vaccinia showed a dose- and time-dependent induction of apoptosis when stimulated with antigenic peptide or H-2Dd/peptide tetramers. • Restimulated CTL showed an upregulation of CD3-chain phosphorylation in comparison to cells stimulated with target cells, indicative of TCR-mediated apoptosis. Furthermore, apoptosis was inhibited by cyclosporin A and U0126, a mitogen activated kinase inhibitor specific for the ERK1/ERK2 MAPK kinase pathway, and a caspase 3 inhibitor.				
gp160 (311–320)	gp160 (318–327 IIIB)	RGPGRAFVTI	Vaccine	murine (L^d)	Tobery1997
	Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* env, nef • An HIV-1 Env vaccine was targeted for rapid cytoplasmic degradation • The rapidly degraded form rapidly stimulated CTL to this peptide, faster than the normal vaccinia-env • The rapidly degraded form also stimulated greater specific CTL lysis and higher CTLp frequencies than normal Env • Similar results were obtained for a Nef protein designed for rapid degradation				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (312–320)	gp120 (V3 loop) (IIIB)	GPGRAFVTI	Vaccine	murine (H-2^d)	Vázquez Blomquist2002
	Vaccine *Vector/Type:* fowlpoxvirus *Strain:* LR150, IIIB, JY1, RF, MN, BRVA *HIV component:* concatonated 15 mer sections of six V3 loops				
	• BALB/c mice were vaccinated with a polyepitope V3 vaccine in a fowlpoxvirus carrying concatonated 15 mer sections of the V3 loops of HIV-1 isolates LR150, JY1, RF , MN, BRVA and IIIB with 5-aa linkers between, fused to the N-term of p64K protein from Neisseria meningitidis.				
	• Intraperitoneal immunization elicited the strongest V3-specific IFN-gamma response in splenocytes, compared to intravenous and subcutaneous immunization. Intraperitoneal immunization conferred protection in a recombinant vaccinia virus challenge model.				
	• The immunodominant response was directed against the IIIB peptide (the IIIB immunizing peptide was SIRIQRGPGRAFVTI, the peptide used to probe the response by Elispot was GPGRAFVTI).				
	• Low CTL responses were also detected to the LR150 (SRGIRIGPGRAILAT) and RF (RKRITMGPGRVYYTT) peptides, no responses were detected to the JY1 (RQSTPIGLGQALYTT), BRVA (RKSITKGPGRVIYAT), or MN (RKRIHIGPGRAFYTT) peptides.				
gp160 (314–322)	gp120 (314–322)	GRAFVTIGK	Peptide-HLA interaction	human (B27)	Jardetzky1991
	• Study of peptide binding to HLA-B27				
gp160 (337–361)	gp120 (337–368 LAI)	KWNNTLKQIDSKLREQFGN-NKTIIF	Vaccine	human (CD4+ CTL)	Johnson1994a
	Vaccine *Vector/Type:* vaccinia *HIV component:* gp160				
	• CD4+ CTL clones were obtained from an HIV-1 vaccinia-env vaccinee				
gp160 (339–354)	gp120 (339–361 LAI)	NNTLKQIDSKLREQFG	Vaccine	human (CD4+ CTL)	Johnson1994b
	Vaccine *Vector/Type:* vaccinia *HIV component:* gp160				
	• CD4+ CTL isolated from LAI IIIB gp160 vaccinees				
gp160 (340–348)	gp120 (346–354 CM243 subtype CRF01)	RVLKQVTEK	HIV-1 infection	human (A11)	Sriwanthana2001
	• Epitope name: E340-348				
	• This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand				
	• HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed				
	• This epitope was weakly reactive in HIV+ control study subject 053 who carried HLA-A11				
gp160 (340–348)	gp120 (346–354 CM243 subtype CRF01)	RVLKQVTEK	HIV-1 infection	human (A11)	Bond2001
	• HLA-A11 CRF01 (called subtype E in Bond et al.) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive				
	• 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 finding and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified				
	• This is one of the new A11 epitopes identified through the streamlined EpiMatrix method, and 2/8 tested FSWs recognized it				
	• This epitope was not conserved in other subtypes, and exact matches were rare				
gp160 (340–349)	gp120 (W6.ID)	NTLKQIVIKL	Vaccine	chimpanzee (Patr-B*14)	Balla-Jhagjhoorsingh1999a
	Vaccine *Vector/Type:* recombinant protein *Strain:* W6.ID *HIV component:* gp120				
	• An HIV-1 rgp120 vaccine induced strong humoral and cellular immune response in sibling chimpanzees, but only one of the two made a detectable CTL response to this Patr-B*14 restricted immunodominant epitope				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (369–375)	gp120 (374–380 BRU)	PEIVTHS	HIV-1 infection	human (A2)	Dadaglio1991
	• Defined through blocking CTL activity, and Env deletions				
gp160 (375–383)	gp120 (379–387 LAI)	SFNCGGEFF	HIV-1 infection	human (B*1516)	Brander2001
	• C. Brander notes this is a B*1516 epitope				
gp160 (375–383)	gp120 (375–383 IIIB)	SFTCGGEFF	HIV-1 infection	human (B15)	Wilson1999a
	• This study describes maternal CTL responses in the context of mother-to-infant transmission • Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants • An additional variant that gave a positive, though reduced, CTL response: SSTCGGEFF and SFTCGGGFF • SFTCGGGVF was an escape mutant				
gp160 (375–383)	gp120 (375–383 SF2)	SFNCGGEFF	HIV-1 infection	human (B15)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-B15+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 1/1 group 2, and 0/1 group 3				
gp160 (375–383)	gp120 (375–383 IIIB)	SFNCGGEFF	HIV-1 infection	human (B63, B15)	Wilson1997a
	• This is the optimal peptide for two CTL clones that recognize this epitope in the context of two different HLA molecules, Cw4 and B15 • Predominant form in proviral DNA of the individual with B15 restricted CTL was SFTCGGEFF and this was recognized • Recognition of a minor autologous variant (SFNCRGEFF) from the B15 donor was greatly reduced				
gp160 (375–383)	gp120 (376–383 PV22)	SFNCGGEFF	HIV-1 infection	human (C*0401)	Brander2001
	• C. Brander notes this is a C*0401 epitope				
gp160 (375–383)	gp120	SFNCGGEFF	HIV-1 infection	human (Cw*0401, Cw*0407)	Bird2002
	• 4/123 (2 HIV-1 positive, 2 HEPS) Kenyan female sex workers carried the novel allele HLA Cw*0407. • HLA Cw*0407 did not differ from Cw*0401 in the region associated with the binding pocket, and Cw*0407 was shown to cross-present a previously defined Cw*0401 epitope, SFNCGGEFF (gp120).				
gp160 (375–383)	gp120 (376–383 PV22)	SFNCGGEFF	HIV-1 infection	human (Cw4)	Johnson1993
	• Conserved epitope				
gp160 (375–383)	gp120 (376–383 PV22)	SFNCGGEFF	HIV-1 infection	human (Cw4)	Wolinsky1996
	• Longitudinal study of epitope variation in vivo				
gp160 (375–383)	gp120 (376–383)	SFNCGGEFF	HIV-1 infection, HIV-1 exposed seronegative	human (Cw4)	Kaul2001a
	• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure • Among HLA-Cw4 women, 1/2 HEPS and 10/11 HIV-1 infected women recognized this epitope • The dominant response to this HLA allele was to this epitope in 6 of the 10/11 responsive HIV-1 infected women, and not in the HEPS case				
gp160 (376–383)	gp120	FNCGGEFF		human (Cw4)	Rowland-Jones1999
	• CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5 • In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, • HIV-2 sequence: TNCRGEFL – no cross-reactivity [Johnson1993]				
gp160 (376–384)	gp120 (376–384 IIIB)	FNCGGEFFY	HIV-1 infection	human (A29)	Wilson1997a
	• This is the optimal peptide for two CTL clones derived from two different donors • FNCRGEFFY and FNCRGGFFY are major and minor autologous variants in one of the donors, and showed reduced or no stimulatory activity for CTL from the host • The IIIB form and the form FNCAGEFFY were present in the other donor, and the CTL line had reduced activity with the FNCAGEFFY form relative to the index peptide				
gp160 (376–384)	gp120 (376–384 IIIB)	PNCGGEFFY	HIV-1 infection	human (A29)	Wilson1999a
	• This study describes maternal CTL responses in the context of mother-to-infant transmission • Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants • PNCRGEFFY was an escape variant				
gp160 (376–384)	gp120 (376–384 LAI)	FNCGGEFFY	HIV-1 infection	human (A29)	Mollet2000
	• Epitope name: E2 • A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses • In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished • Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change				
gp160 (376–384)	gp120 (376–384)	FNCGGEFFY	HIV-1 infection	human (B8)	Oxenius2000
	• Epitope name: FNC • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable • One of the 7/8 study subjects that were HLA B8 recognized this CTL epitope • Patient SC19(HLA A11/12, B8/44, Cw06/0701, DR3/7, DR52/53, DQ 2/8) had a CTL response to epitopes FLKEKGGL, GEIYKRWII, ACQGVGGPGHK, AVDLSHFLK, and FNCGGEFFY that declined during therapy initiated at day 197				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (376–384)	gp160	FNCGGEFFY	HIV-1 infection	human (B8)	Oxenius2002b
	• Epitope name: FNC • Using previously defined epitopes [Oxenius2000, Oxenius2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI). • STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.				
gp160 (376–387)	gp120 (381–392 BRU)	KNCGGEFFYCNS	HIV-1 infection	human (A2)	Dadaglio1991
	• Defined through blocking CTL activity, and Env deletions				
gp160 (377–387)	gp120 (377–387)	NSGGEFFYSNS		human (A2)	Hickling1990
	• Peptides recognized by class I restricted CTL can bind to class II				
gp160 (383–391)	gp120 (385–393)	FYCNTTQLF	HIV-1 infection	human (A*2402)	Ikeda-Moore1997
	• Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402 • This peptide induced CTL in 1/4 HIV-1+ people tested • FYCNTTQLF bound to A*2402 strongly, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained				
gp160 (410–429)	gp120 (410–429 PV22)	GSDTITLPCRIKQFINMWQE	in vitro stimulation	human (CD4+DRA)	Bouhdoud2000
	• CTL were studied through PBMC stimulation in vitro by gp120 pulsed autologous monocytes. • Human CD4+ CTL clone (Een217) is an MHC class II HLA-DRA restricted CTL clone that can lyse antigen presenting HLA-DRA-transfected murine L cells – natural variants of the epitope resulted in an anergic response • Low concentrations of the HXB2-derived variant (GSDTITLPCRIKQIINMWQK) induced T cell anergy – higher concentrations could induce proliferation and cytotoxic activity • CDC42 (TGDIITLPCRIKQII-NRWQV), Eli (TNTNITLQCRIKQIIKMVAG) and Z3 (CTGNITLPCRIKQIIMNWQE) variants did not induce proliferation, cytotoxic or anergic responses				
gp160 (416–424)	Env (413–421 SF2)	LPCRIKQII	HIV-1 infection	human (B*5101)	Tomiyama1999
	• HLA-B27, -B51, and -B57 are associated with slow progression to AIDS, while HLA-B35, -B8, -B24 are associated with a rapid progression to AIDS (Nat. Med. 2:405, 1996;Lancet 22:1187, 1986;Hum Immunol 22:73, 1988;Hum Immunol 44:156, 1995) • 15% of Japanese populations carry HLA-B51 while HLA-B27 and -B57 are detected in less than 0.3% • Of the 172 HIV-1 peptides with HLA-B*5101 anchor residues, 33 bound to HLA-B*5101, seven of these peptides were reactive with CTL from 3 B*5101 positive individuals, and six were properly processed • Four of the six epitopes were highly conserved among B subtype sequences, LPCRIKQII is not conserved				
gp160 (416–424)	gp160 (416–424 LAI)	LPCRIKQII		human (B*5101)	Brander2001
	• C. Brander notes this is a B*5101 epitope				
gp160 (416–424)	gp120 (378–385)	LPCRIKQII	HIV-1 infection, HIV-1 exposed seronegative	human (B51)	Kaul2001a
	• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (416–429)	gp120 (410–429 H3DCG)	LPCRIKQFINMWQE	HIV-1 infection	human (DR4 CD4+)	Siliciano1988
• CD4+ CTL restricted by class II HLA-DR4, targets primed by CD4 mediated uptake of gp120					
gp160 (416–435)	gp120 (421–440 LAI)	LPCRIKQFINMWQEVGKAMY	HIV-1 infection	human (A2)	Dadaglio1991
• Defined through blocking CTL activity, and Env deletions					
gp160 (419–427)	gp120 (424–432 HXB2)	RIKQIINMW		human (A*3201)	Harrer1996b
• C. Brander notes that this is an A*3201 epitope in the 1999 database					
gp160 (419–427)	gp120 (419–427 HXB2)	RIKQIINMW		human (A*3201)	Brander2001
• C. Brander notes this is an A*3201 epitope					
gp160 (419–427)	gp120 (419–427)	RIKQIINMW?	HIV-1 infection	human (A29, A32)	Betts2000
• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes • 1/11 of the A2+ individuals was A29 and responded to RIKQIINMW, and another responder was A32 and these are thought to be presenting molecules • The sequence is unclear – Betts calls both peptide 30 and peptide 32 gp120 419–427 and the peptide sequences are not provided					
gp160 (419–427)	gp120 (424–432 LAI)	RIKQFINMW	HIV-1 infection	human (A32)	Ray1998
• Autologous virus was used to detect CTL in two individuals, and in both cases strain-specific autologous CTL were found • The autologous epitope sequence was RIKQIINMW, MN and RF were KIKQFINMW and RIKQFVNMW respectively, and all were reactive with CTL clones					
gp160 (419–427)	gp120 (420–428)	RIKQIINMW	HIV-1 infection	human (A32)	Ferris1999
• This epitope is processed by a TAP1/2 dependent mechanism					
gp160 (419–427)	gp120	RIKQIINMW	HIV-1 infection	human (A32)	Altfeld2002
• Epitope name: A32-RW10(gp120) • Peripheral blood (PB) and lymph node (LN) CD8+ T-cell responses were compared in 15 asymptomatic HIV-1 infected patients using all known optimal CTL epitopes (http://hiv-web.lanl.gov/content/hiv-db/REVIEWS/brander2001.html) for each person's class I HLA alleles. • 60 epitope responses were detected in both PB and LN samples of the 15 patients, and an additional 8 responses were detected only in LN. The total magnitude of the response was similar in LN and PB, but the percentage of CD8+ T cells in the LN is lower so the number of HIV-specific cells per million CD8+ T-cells is higher in the LN. • 1 year post-HAART treatment in five patients studied, the magnitude of the CD8 T-cell response was decreased in both LN and PB, but more dramatically in PB, and 13/25 epitope responses in the PB became undetectable, in contrast to 5/26 in the LN. • Treatment interruption following HAART induced resulted in increased viremia accompanied by the restoration of the detection of 13 epitopes that had become undetectable in the PB, and the addition of 9 novel epitope responses. • Breakdowns of epitope responses were shown for 4 individuals. Patient B displayed the greatest response to epitope B44-AW11(p24) and also responded to A32-PW10(RT) in both PB and LN samples, while a third response against epitope A32-RW10(gp120) was only detected in the LN sample. Patient D displayed the greatest response to B27-KK10 (p24), and also responded to A30-RY11(p17), A32-PW10(RT), A30-KY11(RT), A32-RW10(gp120), and B18-YY9(Nef).				
gp160 (421–435)	gp120 (421–440 LAI)	KQFINMWQEVGKAMY	HIV-1 infection	human (A2)	Dadaglio1991
• Defined through blocking CTL activity, and Env deletions					

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (421–436)	gp120 (428–443 IIIB)	KQIINMWQEVGKAMYA	HIV-1 exposed seronegative	human	Pinto1995
	• CTL and T helper cell reactivity in healthcare workers exposed to HIV				
gp160 (421–436)	gp120 (MN)	KQIINMWQEVGKAMYA	HIV-1 infection	chimpanzee	Lubeck1997
	• Epitope-specific CTL detected in chimpanzees immunized with adenovirus-HIV-1 MN gp160 recombinant • CTL response may account for protection against subsequent HIV-1 SF2 challenge in a chimpanzee lacking neutralizing antibodies • Helper and cytotoxic T cells can be stimulated by this peptide (T1)				
gp160 (421–436)	gp120 (428–443 IIIB)	KQIINMWQEVGKAMYA	HIV-1 infection	human (A2)	Clerici1991a
	• Helper and cytotoxic T cells can be stimulated by this peptide (T1)				
gp160 (421–436)	gp120 (428–443 IIIB)	KQIINMWQEVGKAMYA	HIV-1 infection	human (A2)	Cease1987
	• Helper and cytotoxic T cells can be stimulated by this peptide (T1)				
gp160 (421–436)	gp120 (428–443 IIIB)	KQIINMWQEVGKAMYA	Vaccine	murine (H-$2^{a,b,f}$)	Shirai1992
	Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* gp160 • In a murine system multiple class I molecules can present to CTL				
gp160 (432–451)	gp120 (439–458 IIIB)	KAMYAPPISGQIRCSSNITG	Vaccine	Rhesus macaque	Wagner1998b
	Vaccine *Vector/Type:* virus-like particle *HIV component:* gag, gp120, V3, CD4BS • A VLP is a non-infectious virus-like particle self-assembled from HIV Pr55 gag – macaques were immunized with VLPs bound to either gp120 or V3+CD4 linear domains Gag and Env specific CTL were stimulated in each case, and Ab response to gag and gp120 was elicited, but the gp120 neutralizing response occurred only with whole gp120, not V3+CD4 – despite the CTL and Ab response, immunized macaques were infected by intervenous challenge with SHIV chimeric challenge stock • CTL specific for this epitope could be found both before and after SHIV challenge				
gp160 (434–443)	gp120 (431–440)	MYAPPIGGQI	Vaccine	murine (H-$2K^d$)	Duarte1996
	Vaccine *Vector/Type:* peptide • Tolerization of CTL response with continued administration of soluble peptide				
gp160 (435–443)	Env (89.6)	YAPPISGQI	Vaccine	Rhesus macaque	Barouch2000, Shen2000
	Vaccine *Vector/Type:* DNA *Strain:* 89.6 *HIV component:* SIVmac239 Gag and HIV-1 89.6P Env *Adjuvant:* IL2/Ig • Epitope name: p41A • Monkeys that received the DNA vaccines augmented with IL-2/Ig were infected when challenged with pathogenic SHIV-89.6P, but had potent CTL responses, stable CD4+ T-cell counts, preserved virus-specific CD4+ T-cell responses, low to undetectable viral loads, and no evidence of disease or mortality by day 140 after challenge – monkeys that got a sham vaccine had high viral load, progressed to disease, and were half were dead by day 140 • IL2/Ig consisting of interleukin-2 (IL-2) for immune stimulation, and the Fc portion of immunoglobulin G (IgG) for stability, was delivered either as protein or as DNA – both enhance the CTL response to vaccination, DNA IL2/Ig giving the most intense response • Responses to a dominant Mamu A*01 gag epitope SIV Gag p11C (CTPYDINQM) and a subdominant epitope HIV-1 Env p41A (YAPPISGQI) were tracked and had good durability prior to challenge, and the higher the prechallenge peak p11C CTL response, the lower the post-challenge viral load • No NAb responses were detected in the vaccinated monkeys prior to challenge, and comparable peak NAb titers developed in vaccinated monkeys and control monkeys with preserved CD4+ T-cells • Shen et al. 2000 is an accompanying commentary				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (435–443)	Env (89.6)	YAPPISGQI	Vaccine	Rhesus macaque	Barouch2001b
Vaccine *Vector/Type:* vaccinia *Strain:* 89.6 *HIV component:* SIVmac239 Gag/Pol and HIV-1 89.6P Env *Adjuvant:* IL2/Ig • Epitope name: p41A • Four monkeys were vaccinated with a modified vaccinia Ankara (MVA) vaccine that elicited strong CTL to the immunodominant SIV gag eptiope in 4/4 animals, and 1/4 made a response to the HIV Env epitope YAPPISGQI, as determined by tetramer staining and chromium release assays • The animals were infected when challenged with pathogenic SHIV-89.6P, but had potent CTL responses, secondary NAb responses upon challenge, partial preservation of CD4+ T-cell counts, lower viral loads, and no evidence of disease or mortality by day 168 after challenge – monkeys that got a sham vaccine had high viral load, progressed to disease, and 2/4 were dead by day 168				
gp160 (435–443)		YAPPISGQI	SHIV infection	Rhesus macaque (Mamu A*01)	Egan1999
• SHIV-infected rhesus macaques have high frequencies of response to the SIVmac epitope gag p11C,C-M (CTPYDINQM) but only a fraction of A*01 monkeys tested have responses to SIVmac pol epitope STPPLVRLV and HIV-1 env epitope YAPPISGQI					
gp160 (435–443)	gp41 (89.6)	YAPPISGQI	SHIV infection, Vaccine	Rhesus macaque (Mamu A*01)	Barouch2001a
Vaccine *Vector/Type:* vaccinia MVA, DNA *Strain:* 89.6, HXBc2 *HIV component:* SIV Gag and HIV-1 Env *Adjuvant:* IL2/Ig • Epitope name: p41A • Mamu-A*01+ rhesus monkeys infected with SHIV-89.6 and SHIV-HXBc2 make immunodominant responses to SIV Gag p11C epitope (CTPYDINQM) and a subdominant response to HIV-1 Env p41A epitope (YAPPISGQI) • The binding affinities are the same for the two Mamu A*01 epitopes, so that is not what dictates the dominance. • Monkeys vaccinated with MVA vectors carrying SIV gag/pol and HIV-1 env showed the same p11C epitope dominance and p41A epitope subdominance, but co-dominance was observed and the response to p41A increased when DNA vaccination was done using the SIV and HIV genes under CMV promotor control with IL2-IG adjuvant				
gp160 (444–453)	Env	RCSSNITGLL		human (B56)	De Groot2001
• The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes • A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 of the predicted B7 superfamily (HLA B7, B8, and B58) epitopes were identified that could stimulate IFNγ production in an ELISPOT assay • RCSSNITGLL was newly defined as an epitope in this study, and was shown to stimulate an ELISPOT response, despite not detectably binding to HLA-B7					
gp160 (489–508)	Env (496–506 BH10, LAI)	VKIEPLGVAPTKAKRRVVQR	HIV-1 infection	human	Maksiutov2002
• This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins. • This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is VAPTKAKRRVV) has similarity with the mast/stem cell growth factor receptor precursor fragment VVPTKADKRRSV.					
gp160 (489–508)	Env (497–512 BH10, LAI)	VKIEPLGVAPTKAKRRVVQR	HIV-1 infection	human	Maksiutov2002
• This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins. • This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is APTKAKRRVVQREKRA) has similarity with the human interferon-related IFRD2 (PC4-B) protein fragment ARTKARSRVRDKRA.					

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (489–508)	gp120 (494–513 BRU)	VKIEPLGVAPTKAKRRVVQR	HIV-1 infection	human (A2)	Dadaglio1991
	• Defined through blocking CTL activity, and Env deletions				
gp160 (519–543)	gp41 (519–543)	FLGFLGAAGSTMGAASLTL–TVQARC	HIV-1 infection	human (Cw7)	Nehete1998a
	• Three long-term non-progressors and one asymptomatic HIV+ individual were studied and found to have HLA class I C-restricted CD8+ Env-specific CTLs – Cw7 specific CTL were found against three peptides, including this one • HLA-C antigens are expressed on lymphoid cells to a lesser extent, 10% of either HLA-A or HLA-B • HLA-C confers protection against lysis by natural killer cells and by non-MHC-restricted effector T cells and Cw7 directly governs this resistance to lysis – the authors hypothesize that pathogens that inhibit antigen expression and class I expression may particularly down regulate Cw7, thus triggering non-MHC restricted killing				
gp160 (552–571)	Env (552–571)	QSNLLRAIEAQQHMLQLTVW	HIV-1 infection	human	Novitsky2002
	• HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
gp160 (557–565)	gp41 (557–565 IIIB)	RAIEAQQHL	HIV-1 infection	human	Wilson1996
	• Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study • RAIDAQQHL and RVIEAQQHL, naturally occurring variants, were found in mother and are recognized				
gp160 (557–565)	gp41 (557–565)	RAIEAQQHL	HIV-1 infection	human	Betts2000
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes • 1/11 of the A2+ individuals was HLA A*0201, A32, B60, B78, and responded to RAIEAQQHL, previously noted to be B51				
gp160 (557–565)	gp41 (557–565 IIIB)	RAIEAQQHL	HIV-1 infection	human	Wilson1999a
	• This study describes maternal CTL responses in the context of mother-to-infant transmission • Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants • This epitope was invariant in both the mother and her infant				
gp160 (557–565)	Env (555–567 BH10, LAI)	RAIEAQQHL	HIV-1 infection	human	Maksiutov2002
	• This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins. • This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is LLRAIEAQQHLL) has similarity with human MHC class II regulatory factor RFX1 fragment LLRLMEDQQHMA.				
gp160 (557–565)	gp41 (557–565 IIIB)	RAIEAQQHL	HIV-1 infection	human (B*5101)	Brander2001
	• C. Brander notes this is a B*5101 epitope				
gp160 (557–565)	gp41 (557–665)	RAIEAQQWQ	HIV-1 infection	human (B*5101)	Samri2000
	• Epitope name: E3 • The epitope was recognized by patient 246#1 in a study of the effects of therapy escape mutations on CTL recognition				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (557–565)	gp41 (557–565 IIIB)	RAIEAQQHL	HIV-1 infection	human (B51)	Sipsas1997
	• HIV IIIB proteins were used to define the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB • KAIEAQQHL, a variant found in HIV-1 NY5CG, was also recognized • RAIEAQQHM, a variant found in HIV-1 JRCSF, was also recognized • RAIDAQQHL, a variant found in HIV-1 ETR, was also recognized • RAIKAQQHL, a variant found in HIV-1 CDC42, was also recognized				
gp160 (557–565)	gp41 (557–565)	RAIEAQQHL	HIV-1 infection	human (B51)	Ferris1999
	• This epitope can be processed by a TAP1/2 dependent mechanism				
gp160 (557–565)	gp41 (557–565)	RAIEAQQWQ	HIV-1 infection	human (B51)	Oxenius2000
	• Epitope name: RAI • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable • None of the 8 study subjects recognized this epitope but none were HLA B51+				
gp160 (557–565)	gp41 (47–55)	RAIEAQQHL	HIV-1 infection	human (B51)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
gp160 (557–565)	gp41 (557–565 LAI)	RAIEAQQHL	HIV-1 infection	human (B51)	Mollet2000
	• Epitope name: E3 • A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses • In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished • Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change				
gp160 (557–565)	Env (gp160) (557–565)	RAIEAQQHL	HIV-1 infection	human (Cw*0304)	Currier2002a
	• Cross-reactive responses were found in PBMC isolated from individuals infected with either B or CRF01_AE clade viruses, as determined by Elispot assays of target cells expressing recombinant vaccinia viruses expressing HIV-1 gag, env, nef and pol from many clades. • CTL from subject US101, infected with a clade B virus, displayed broad cross-reactivity to HIV-1 clade A, B, C, D, CRF01_AE, F G, recognized this epitope. Clade B and C had a L->M change in the C-term position that was tolerated. The H clade Env was not cross-reactive, and had the sequence RAIAARQHM.				
gp160 (565–573)	Env (731–739)	LLQLTVWGI	HIV-1 infection	human (A2 supertype)	Propato2001
	• Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This epitope can bind four of the five HLA-A2 supertypes alleles (A*0201, A*020 2, A*0203, A*0206 and A*6802)				
gp160 (570–589)	gp41 (571–590 LAI)	VWGIKQLQARILAVERYLKD	Vaccine	human (CD4+ CTL(DR-1))	Kent1997a
	Vaccine *Vector/Type:* vaccinia prime with rgp160 boost *Strain:* LAI *HIV component:* gp160 • VWGIKQLQARILAVERYLKD, present in HIV-1 LAI, was the immunizing strain • VWGIKQLQARVLAVERYLKD, present in HIV-1 MN, was also recognized • VWGIKQPQARVLAVERYLRD was the form carried by the autologous strain that infected the vaccinee • Lysis of the target cells by CD4+ CTL was inhibited with the addition of the peptide representing the autologous strain • The infecting virus epitope also antagonized the proliferative functions of the CD4+ CTL clone • The behavior of the autologous strain presents a possible mechanism for vaccine failure since the infecting virus not only escapes CTL activity, but inhibits the ability of CTL to recognize other variants				
gp160 (572–590)	gp41 (572–590 BRU)	GIKQLQARILAVERYLKDQ	Vaccine	human (DPw4.2)	Hammond1991
	Vaccine *Vector/Type:* recombinant protein *Strain:* BRU *HIV component:* gp160 • CD4+ CTL				
gp160 (575–599)	gp41 (575–599 IIIB)	QLQARILAVERYLKDQQLL-GIWGCS	HIV-1 infection	human (B14)	Jassoy1992
	• Epitope recognized by CTL clone derived from CSF				
gp160 (583–592)	gp41 (583–592 PV22)	VERYLKDQQL	HIV-1 infection	human (B14)	Jassoy1993
	• HIV-1 specific CTLs release γ-IFN, and α- and β-TNF				
gp160 (584–592)	gp41 (584–592)	ERYLKDQQL	HIV-1 infection	human	Price1995
	• Study of cytokines released by HIV-1 specific activated CTL				
gp160 (584–592)	gp41 (584–592)	ERYLKDQQL	HIV-1 infection	human	Borrow1994
	• Three out of five patients with HIV-1 symptomatic infection controlled their viral infection well and mounted an early, strong HIV-1 specific MHC restricted CTL response • One of the three, study subject BORI, specifically recognized this peptide				
gp160 (584–592)	gp41 (584–592 HXB2)	ERYLKDQQL	HIV-1 infection	human (A32, B14)	Mollet2000
	• Epitope name: E4 • A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses • In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished • Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change				
gp160 (584–592)	gp41	ERYLRDQQL	HIV-1 infection	human (B*14)	Kaul2002
	• Neisseria gonorrhea cervititis in 9 HIV+ Kenyan sex workers caused a functional deficiency in IFN-gamma production in HIV-1 epitope-specific CD8+ T-cells, detected by intracellular cytokine production and tetramer assays, while not affecting the total number of epitope-specific CTLs.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Ghonorrhea caused the weaker HIV-1 specific CTL responses in 4 HIV-1 exposed persistently seronegative (HEPS) women to become undetectable by Elispot and tetramer assays, and CMV-specific CTL in 2 HEPS subjects were shown to have impaired function with regard to IFN-gamma production.				
gp160 (584–592)	gp41 (584–592 PV22)	ERYLKDQQL	HIV-1 infection	human (B*1402)	Brander2001
	• C. Brander notes this is a B*1402 epitope				
gp160 (584–592)	gp41	ERYLKDQQL	HIV-1 infection	human (B14)	Wagner1998a
	• CTL specific for HIV epitopes were used to show that the mediators of both the cytolytic (granzyme A was used as the marker) and non-cytolytic (HIV-1 inhibitory chemokines MIP-1 α and RANTES were used as markers) anti-viral responses are localized within the CTL's cytotoxic granules				
gp160 (584–592)	gp41 (584–592)	ERYLKDQQL	HIV-1 infection	human (B14)	Kalams1999b
	• Two patients were followed before and after HAART – reduced plasma HIV-1 RNA levels resulted in a decline in HIV in vivo activated specific CTL such that by day 260 CTL activities were undetectable • ERYLKDQQL was the dominant response in one of the individuals, SLYNTVATL subdominant • Sporadic breakthrough in viremia resulted in increases in CTLp • Peptide-tetramer staining demonstrated that declining levels of in vivo-activated CTL were associated with a decrease in expression of CD38 • Memory CTL frequency directed against Vac-Gag, Vac-RT, Vac-Env, and Vac-Nef initially increased with HAART and then decreased with the decline of the viral load				
gp160 (584–592)	gp41 (591–599 SF2)	ERYLKDQQL	HIV-1 infection	human (B14)	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • Eleven subjects had CTL that could recognize vaccinia-expressed LAI gp160 • One of these 11 had CTL response to this peptide • The responding subject was HLA-A3, -A32, -B7, -B14				
gp160 (584–592)	gp41 (591–599 SF2)	ERYLKDQQL	HIV-1 infection	human (B14)	Cao1997a
	• The consensus sequence for clades B, C, and D is ERYLKDQQL • The consensus sequence for clade A is ERYLRDQQL and it is equally reactive • The consensus sequence for clade E is ERYLKDQKF and it is not reactive				
gp160 (584–592)	gp41	ERYLKDQQL	HIV-1 exposed seronegative	human (B14)	Rowland-Jones1998a
	• A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating • The A and D subtype consensus are identical to the B clade epitope, ERyLkDQQL				
gp160 (584–592)	gp41 (584–592)	ERYLKDQQL	HIV-1 infection	human (B14)	Sipsas1997
	• HIV IIIB proteins were used to define the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB				
gp160 (584–592)	gp41 (584–592)	ERYLKDQQL	HIV-1 infection	human (B14)	Yang1996
	• CD4+ cell lines acutely infected with HIV were studied to determine their susceptibility to lysis by CTL • Clones specific for RT lysed HIV-1 infected cells at lower levels than Env or Gag specific clones • The distinction was thought to be due to lower expression of RT relative to Env and Gag • CTL can lyse infected cells early after infection, possibly prior to viral production				
gp160 (584–592)	gp41 (584–592)	ERYLKDQQL	HIV-1 infection	human (B14)	Yang1997a
	• CTL inhibit HIV-1 replication at effector cell concentrations comparable to those found in vivo				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• CTL produced HIV-1-suppressive soluble factors – MIP-1α, MIP-1β, RANTES, after antigen-specific activation • CTL suppress HIV replication more efficiently in HLA-matched cells				
gp160 (584–592)	gp41 (584–592 PV22)	ERYLKDQQL	HIV-1 infection	human (B14)	Johnson1992
	• Two overlapping CTL epitopes were mapped with different HLA restriction (also see YLKDQQLL HLA-B8)				
gp160 (584–592)	gp41 (584–592 PV22)	ERYLKDQQL	HIV-1 infection	human (B14)	Jassoy1993
	• HIV-1 specific CTLs release γ-IFN, and α- and β-TNF				
gp160 (584–592)	gp41 (584–592 HXB2)	ERYLKDQQL	HIV-1 infection	human (B14)	Kalams1994, Kalams1996
	• Longitudinal study of T cell receptor usage in a single individual • Persistence of oligoclonal response to this epitope for over 5 years				
gp160 (584–592)	gp41 (584–592)	ERYLKDQQL	Peptide-HLA interaction	human (B14)	DiBrino1994a
	• Epitope studied in the context of HLA-B14 binding				
gp160 (584–592)	gp41 (584–592)	ERYLKDQQL	HIV-1 infection	human (B14)	Hammond1995
	• This peptide can be processed for HLA-B14 presentation in a TAP-1/2 independent pathway				
gp160 (584–592)	gp41 (584–592)	ERYLKDQQL	HIV-1 infection	human (B14)	Kalams1996
	• CTL response to this epitope was studied in 5 HLA-B14 positive persons • CTL responses were detected in all five, and CTL clones were isolated from 4/5 • A diverse repertoire of TCRs recognized this epitope, with similar fine specificities • 3/5 subjects showed no variation in viral sequence, 2/5 had a dominant variant that resulted in poor recognition, ERYLQDQQL • A minor CTL response specific for the ERYLQDQQL could be detected by two individuals, but the major CTL response was to the ERYLKDQQL form even when it was the minority form • Some single amino acid substitutions were well tolerated by most of the CTL clones tested, but others, particularly in the center three amino acid positions, abrogated peptide stimulatory activity				
gp160 (584–592)	gp120 (584–592)	ERYLKDQQL	HIV-1 infection	human (B14)	Ferris1999, Hammond1995
	• This epitope is processed by both TAP1/2 dependent and independent mechanisms				
gp160 (584–592)	gp41	ERYLKDQQL		human (B14)	Rowland-Jones1999
	• CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5 • In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, and the B35 allele seems to be protective • HIV-2 sequence: EKYLQDQAR – no cross-reactivity [Johnson1992]				
gp160 (584–592)	gp41 (SF2)	ERYLKDQQL	HIV-1 infection	human (B14)	Goulder2001a
	• Epitope name: EL9 • Data from patient AC13 suggest a role for this epitope in initial control of viremia in acute infection, as it is one of several subdominant CTL epitopes recognized during the initial decline in viremia • A CTL response to SL9, SLYNTVATL, was not evident until 18 months post-presentation • Recognized by two A*0201-positive chronically infected subjects				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (584–592)	gp41 (584–592)	ERYLKDQQL	HIV-1 infection	human (B14)	Islam2001
• Epitope name: 588K • Transcript frequencies of four CTL clones from patient 115, with a chronic and stable HIV-1 infection, were tracked in a longitudinal study of samples collected 6-11 years post infection: clone M21 and E15 recognize ERYLKDQQL,and clone D87 recognizes variant ERYLQDQQL, and clone p175b recognizes the A2 epitope SLYNTVATL • CTL clone M21 uses the Vbeta 4, CDR3 VKDGA, Jbeta 1.2 TCR beta gene, and clone E15 uses the Vbeta 4, CDR3 VEDWGGAS Jbeta 2.1 TCR beta gene, and D87 uses Vbeta8, ALNRVD, Jbeta2.1 • Responses were stable even through HAART with undetectable viral loads but frequencies varied over time by 100-fold, ranging from 0.012% of the total population for SLYNTVATL at its lowest point to 3.78% for M21, with the relative frequencies of clones shifting over time					
gp160 (584–592)	gp41 (589–597 SF2)	ERYLKDQQL	HIV-1 infection	human (B14)	Altfeld2001b
• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-B14+ individuals that had a CTL response to this epitope broken down by group: 3/3 group 1, 1/2 group 2, and 0/0 group 3					
gp160 (584–592)	gp41 (589–597)	ERYLRDQQL	HIV-1 infection, HIV-1 exposed seronegative	human (B14)	Kaul2001a
• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers					
gp160 (584–592)	gp41 (JRCSF)	ERYLKDQQL	HIV-1 infection	human (B14)	Severino2000
• Primary HLA-B14+ CD4+ CD3+ and HLA-mismatched lymphocytes from uninfected donors were infected with JRCSF after isolation then cocultured with the B14-restricted CTL clone 15160/D75 specific for ERYLKDQQL, and viral inhibition was MHC-restricted • Primary monocytes and monocyte-derived DC were generated from the same donors, replication of HIV-1 in these cell types was less efficient than in lymphocytes and could also be inhibited by MHC-restricted CTL • DC-lymphocyte cluster cultures allowed vigorous viral replication and MHC-restricted CTL viral inhibition was blunted or lost depending on the ratio of DC to CD4+ lymphocyte in the culture					
gp160 (584–592)	gp41 (SF2)	ERYLKQQL	HIV-1 infection	human (B14)	Altfeld2000b
• This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual					
gp160 (584–592)	Env (589–597)	ERYLKDQQL	HIV-1 infection	human (B14)	Guillon2002
• An early-expressed Nef protein was modified to contain Env and Pol epitopes to enable the study the effect of expression kinetics on CTL mediated suppression of replication. The "EpiNef" construct was inserted into a recombinant vaccinia virus which was used to infect a target cell line; the target cells were lysed by CTL clones specific for the Env and Pol epitopes indicating that they were properly processed.					

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (584–592)	gp41 (584–592)	ERYLKDQQL	HIV-1 infection	human (B14)	Yang2002
• Nef down-modulates class I protein expression, and this study demonstrates directly that Nef-deleted HIV-1 NL-43 can be more effectively killed in vitro than NL-43 with an intact Nef. The effect was shown to be specific for class I presentation of epitopes, and unlike Nef, deleting Vpr did not alter CTL susceptibility of NL43 infected cells. The CTL clone 15160D75, specific for the class I B14 presented epitope ERYLKDQQL, was one of four used in this study.					
gp160 (584–592)	gp41	ERYLKDQQL	HIV-1 infection	human (B14)	Altfeld2002
• Epitope name: B14-EL9(gp41) • Peripheral blood (PB) and lymph node (LN) CD8+ T-cell responses were compared in 15 asymptomatic HIV-1 infected patients using all known optimal CTL epitopes (http://hiv-web.lanl.gov/content/hiv-db/REVIEWS/brander2001.html) for each person's class I HLA alleles. • 60 epitope responses were detected in both PB and LN samples of the 15 patients, and an additional 8 responses were detected only in LN. The total magnitude of the response was similar in LN and PB, but the percentage of CD8+ T cells in the LN is lower so the number of HIV-specific cells per million CD8+ T-cells is higher in the LN. • 1 year post-HAART treatment in five patients studied, the magnitude of the CD8 T-cell response was decreased in both LN and PB, but more dramatically in PB, and 13/25 epitope responses in the PB became undetectable, in contrast to 5/26 in the LN. • Treatment interruption following HAART resulted in increased viremia accompanied by the restoration of the detection of 13 epitopes that had become undetectable in the PB, and the addition of 9 novel epitope responses. • Breakdowns of epitope responses were shown for 4 individuals. Patient A displayed the greatest response to epitope B14-EL9(gp41), a strong response to B7-TL9(p24), and responses to B7-TM9(Nef) and A32-PW10(RT).					
gp160 (584–592)	gp41	ERYLKDQQL	HIV-1 infection, Vaccine	human (B14)	Hanke2000, Wee2002
Vaccine *Vector/Type:* DNA prime with vaccinia MVA boost *Strain:* subtype A *HIV component:* p17, p24, polyepitope • The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000]. • Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].					
gp160 (584–592)	gp41 (subtype B)	ERYLKDQQL	HIV-1 exposed seronegative	human (B14, B*1402)	Rowland-Jones1998b
• HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes • This epitope is conserved among B and D clade viruses • The Clade A version of the epitope is ERYLRDQQL					
gp160 (585–592)	gp41 (584–591 SF2)	RYLRDQQL	HIV-1 infection	human (A*2402)	Ikeda-Moore1997
• Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402					

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This peptide induced CTL in 2/4 HIV-1+ people tested • RYLRDQQL bound to A*2402 weakly, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained				
gp160 (585–592)	gp41 (590–597 LAI)	RYLKDQQL	HIV-1 infection	human (B27)	Shankar1996
gp160 (585–593)	gp41 (584–591 SF2)	RYLRDQQLL	HIV-1 infection	human (A*2402)	Ikeda-Moore1997
	• Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402 • This peptide induced CTL in 4/4 HIV-1+ people tested • RYLRDQQLL bound to A*2402 strongly, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained				
gp160 (585–593)	gp41 (591–598 LAI)	RYLKDQQLL		human (A*2402)	Brander2001
	• C. Brander notes this is an A*2402 epitope				
gp160 (585–593)	gp41	RYLKDQQLL	HIV-1 infection	human (A24)	Altfeld2002
	• Epitope name: A24-RL9(gp41) • Peripheral blood (PB) and lymph node (LN) CD8+ T-cell responses were compared in 15 asymptomatic HIV-1 infected patients using all known optimal CTL epitopes (http://hiv-web.lanl.gov/content/hiv-db/REVIEWS/brander2001.html) for each person's class I HLA alleles. • 60 epitope responses were detected in both PB and LN samples of the 15 patients, and an additional 8 responses were detected only in LN. The total magnitude of the response was similar in LN and PB, but the percentage of CD8+ T cells in the LN is lower so the number of HIV-specific cells per million CD8+ T-cells is higher in the LN. • 1 year post-HAART treatment in five patients studied, the magnitude of the CD8 T-cell response was decreased in both LN and PB, but more dramatically in PB, and 13/25 epitope responses in the PB became undetectable, in contrast to 5/26 in the LN. • Treatment interruption following HAART induced resulted in increased viremia accompanied by the restoration of the detection of 13 epitopes that had become undetectable in the PB, and the addition of 9 novel epitope responses. • Breakdowns of epitope responses were shown for 4 individuals. Patient C displayed the greatest response to B27-KK10(p24), and in decreasing order also responded to A24-RW8(Nef), B7-IL9(gp41), A24-RL9(gp41), A24-YL8(gp41), and B7-TM9(Nef).				
gp160 (585–595)	gp41 (584–591 SF2)	RYLRDQQLLGI	HIV-1 infection	human (A*2402)	Ikeda-Moore1997
	• Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402 • This peptide induced CTL in 4/4 HIV-1+ people tested • RYLRDQQLLGI bound to A*2402 with medium strength, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained				
gp160 (585–595)	Env (584–594)	RYLRDQQLLGI	Vaccine	human (A*2402)	Kawana-Tachikawa2002
	Vaccine *Vector/Type:* Sendai virus vector system (SeV) *HIV component:* class I/peptide complexes • Epitope name: Env584-11 • A Sendai virus vector system (SeV) was developd that expressed HLA-A*2402-restricted class I/peptide complexes; this system could be used to detect responses and has the potential to elicit immune responses. • MHC class I/peptide tetramers could be made using this system that bound to epitope-specific CTLs in PBMCs. • Cells transfection with SeV modified to express A*2402-HIV epitope complexes induced CTL mediated specific cell lysis.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (586–593)	gp160	YLRDQQLL	HIV-1 infection	human	Kaul2001c
• This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative • The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire • This epitope was recognized in 1/22 HEPS sex worker controls, ML887					
gp160 (586–593)	gp41 (584–591 NL43)	YLKDQQLL	HIV-1 infection	human (A*2402)	Dai1992
• The lysine (K) is critical for eliciting a HLA-A24 CTL response • C. Brander notes that this is an A*2402 epitope in the 1999 database, and suggested that the epitope is RYLKQQLL					
gp160 (586–593)	gp41 (591–598)	YLRDQQLL	HIV-1 infection, HIV-1 exposed seronegative	human (A24)	Kaul2001a
• Variants (R)YL(R/K)DQQLL are specific for the A/B clade • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure • Among HLA-A24 women, 3/4 HEPS and 10/10 HIV-1 infected women recognized this epitope, and (R)YL(R/K)DQQLL tended to be reactive in HEPS and infected women, RDYVDRFFKTL in infected women only • The dominant response to this HLA allele was to this epitope in all 3/4 HEPS cases but in only 4 of the 10/10 HIV-1 infected women • Differences in epitope specificity were only seen for responses restricted by class I HLA alleles A2, A24, A*6802, B14, and B18, previously shown to be associated with resistance to HIV-1 in this cohort					
gp160 (586–593)	gp41 (580–587 CM243 subtype CRF01)	YLKDQQLL	HIV-1 infection	human (A24)	Bond2001
• More than half of a cohort of HIV+ female sex workers (FSW) from Northern Thailand were HLA-A11 positive, and this study concentrated on A11 epitopes in this group, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested. • The only HLA-A24 FSW tested did not recognized the E clade version of this epitope RYLKDQKLL, which differs from the previously defined B clade version by one amino acid, YLKDQQLL, with an additional amino acid added on					
gp160 (586–593)	gp41 (subtype A)	YLKDQQLL	HIV-1 infection, Vaccine	human, macaque (A24, B8)	Hanke2000, Wee2002
Vaccine *Vector/Type:* DNA prime with vaccinia MVA boost *Strain:* subtype A *HIV component:* p17, p24, polyepitope • The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000].					

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].				
gp160 (586–593)	gp41 (586–593 LAI)	YLKDQQLL	HIV-1 infection	human (A24, B8)	Mollet2000
	• Epitope name: E1 • A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses • In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished • Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change				
gp160 (586–593)	gp41 (586–593)	YLKDQQLL	HIV-1 infection	human (B*0801)	Brander2001
	• C. Brander notes this is a B*0801 epitope				
gp160 (586–593)	gp41 (586–593)	YLKDQQLL	HIV-1 infection	human (B8)	Johnson1992
	• Two overlapping CTL epitopes were mapped with different HLA restriction (also see ERYLKDQQL HLA-B14)				
gp160 (586–593)	gp41 (586–593)	YLKDQQLL	Peptide-HLA interaction	human (B8)	Sutton1993
	• Predicted epitope based on B8-binding motifs, from larger peptide QLQARILAVERYLKDQQLLGIWGCS				
gp160 (586–593)	gp41 (76–83)	YLKDQQLL		human (B8)	Goulder1997g
	• Included in a study of the B8 binding motif				
gp160 (586–593)	gp41	YLKDQQLL		human (B8)	Rowland-Jones1999
	• CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5 • In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive • HIV-2 sequence: YLQDQARL – no cross-reactivity [Johnson1992]				
gp160 (586–593)	gp41 (586–593)	YLKDQQLL	HIV-1 infection, HIV-1 exposed seronegative	human (B8)	Kaul2001a
	• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers				
gp160 (586–593)	gp41 (586–593)	YLKDQQLL	HIV-1 infection	human (B8)	Day2001
	• B8-restricted CTL accounted for about 1/3 of the total CTL response in one individual				
gp160 (586–598)	gp41 (586–598)	YLRDQQLLGIWGC	HIV-1 infection	human (Cw7)	Nehete1998a
	• Three long-term non-progressors and one asymptomatic HIV+ individual were studied and found to have HLA class I C-restricted CD8+ Env-specific CTLs – Cw7 specific CTL were found against three peptides, including this one • HLA-C antigens are expressed on lymphoid cells to a lesser extent, 10% of either HLA-A or HLA-B				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• HLA-C confers protection against lysis by natural killer cells and by non-MHC-restricted effector T cells and Cw7 directly governs this resistance to lysis – the authors hypothesize that pathogens that inhibit antigen expression and class I expression may particularly down regulate Cw7, thus triggering non-MHC restricted killing				
gp160 (594–608)	gp41	GIWGCSGKLICTTAV	HIV-1 infection	human (B57)	Jin1998b
	• Progressive HIV-1 infection and CD4 decline was associated decreased the IL-2-expandable HIV-1 CTL response in 10 asymptomatic HIV-infected patients – this observation may be partially due to a reduction and impaired function of T helper cells, CTL exhaustion and APC dysfunction • Continued presence of HIV-1 specific memory cells (CTLp) was observed in three patients, one to GIWGCSGKLICTTAV, one to ALIWEDLRSLCLFSY, and one to PIPIHYCAPAGFAILKCNNK				
gp160 (606–614)	gp41 (605–615 LAI) **Vaccine** *Vector/Type:* vaccinia *HIV component:* gp160	TAVPWNASW	Vaccine	human (B*3501)	Brander2001
	• C. Brander notes this is a B*3501 epitope				
gp160 (606–614)	gp41 (606–614 HXB2)	TAVPWNASW	HIV-1 infection	human (B*3501)	Ferris1996
	• Natural form of this peptide is not glycosylated, suggesting initial Class I processing may occur in the cytosol				
gp160 (606–614)	gp41 (605–615 LAI) **Vaccine** *Vector/Type:* vaccinia *HIV component:* gp160	TAVPWNASW	Vaccine	human (B35)	Johnson1994b
	• Epitope for vaccine induced CD8+ clone				
gp160 (606–614)	gp41 (606–614 LAI) **Vaccine** *Vector/Type:* vaccinia *HIV component:* gp160	TAVPWNASW	Vaccine	human (B35)	Johnson1994a
	• HLA restricted CTL response to epitope in HIV-1 vaccinia-env vaccinees				
gp160 (606–614)	gp41 (606–614 LAI) **Vaccine** *Vector/Type:* vaccinia *HIV component:* gp160	TAVPWNASW	Vaccine	human (B35)	Hammond1995
	• Peptide only processed by a TAP-1/2-dependent pathway				
gp160 (606–614)	gp41 (606–614)	TAVPWNASW	HIV-1 infection	human (B35)	Ferris1999
	• This epitope is processed by a TAP1/2 dependent mechanism				
gp160 (606–614)	gp41 (subtype B)	TAVPWNASW	HIV-1 exposed seronegative	human (B35)	Rowland-Jones1998b
	• HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes • This epitope is conserved among A, B and D clade viruses				
gp160 (606–614)	gp41 (606–614)	TAVPWNASW	HIV-1 infection, HIV-1 exposed seronegative	human (B35)	Kaul2001a
	• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers				
gp160 (634–648)	gp41 (641–655 SF2)	EIDNYTNTIYTLLEE	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • Eleven subjects had CTL that could recognize vaccinia-expressed LAI gp160				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• One of these 11 had CTL response to this peptide • The responding subject was HLA-A1, A2, B51, and B57				
gp160 (678–686)	Env (679–687 subtype B)	WLWYIKIFI	Vaccine	human (A2.1)	Kundu1998a
	Vaccine *Vector/Type:* recombinant protein *Strain:* MN *HIV component:* gp160 • Ten HIV-1+ HLA A2 asymptomatic individuals were given two courses of HIV-1 MN rgp160 vaccine over a 2 year period • Two hundred and fifty three HIV-1 peptides of 9 or 10 aa possessing the HLA-A2.1 binding motif (Leu at position 2, Val at the C terminus) were identified in gp160, of which 25 had a high or intermediate binding affinity • Eleven peptides were studied that had high HLA-A2 binding affinity – a CTL response was detected to 9/11 peptides in at least 1 individual • CTL responses after reimmunization may include recall responses – only individuals with vaccine cross-reactive sequences prior to vaccination showed detectable CTL responses				
gp160 (680–688)	gp41 (679–687 SF2)	WYIKIFIMI	HIV-1 infection	human (A*2402)	Ikeda-Moore1997
	• Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402 • This peptide induced CTL in 1/4 HIV-1+ people tested • WYIKIFIFMI bound to A*2402 strongly, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained				
gp160 (685–693)	Env (686–694 subtype B)	FIMIVGGLV	Vaccine	human (A2.1)	Kundu1998a
	Vaccine *Vector/Type:* recombinant protein *Strain:* MN *HIV component:* gp160 • Ten HIV-1+ HLA A2 asymptomatic individuals were given two courses of HIV-1 MN rgp160 vaccine over a 2 year period • Two hundred and fifty three HIV-1 peptides of 9 or 10 aa possessing the HLA-A2.1 binding motif (Leu at position 2, Val at the C terminus) were identified in gp160, of which 25 had a high or intermediate binding affinity • Eleven peptides were studied that had high HLA-A2 binding affinity – a CTL response was detected to 9/11 peptides in at least 1 individual • CTL responses after reimmunization may include recall responses – only individuals with vaccine cross-reactive sequences prior to vaccination showed detectable CTL responses • ALTERNATIVE EPITOPE: IMIVGGLVGL – no CTL response was shown to the peptides FIMIVGGLV or IMIVGGLVGL				
gp160 (698–707)	Env (696–706)	VFAVLSIVNR	HIV-1 infection	human (A*3303)	Hossain2001, Takiguchi2000
	• HLA-A33 a very common allele in Asian, with HLA-A*3303 the most common among the Japanese. New A*3303 epitopes were defined to better characterize the immune response in this population. • The anchor motif for HLA*3303 (A, I, L, V, F, Y in position 2 (F and Y bind most strongly), and R (K is also tolerated) in the C-terminal position) was used to define 82 potentially reactive peptides in Env; 37/82 peptides bound to A*3303; 3/37 peptides could induce peptide-specific CTL in bulk PBMC cultures from 1/3 HLA A*3303 positive individuals tested. • CTL clones were isolated that killed target cells in a concentration dependent manner after pulsing with the VFAVLSIVNR peptide, that could also kill cells transfected with env expressed from a vaccinia vector. Bulk cultures were tested from six additional people, and only 1/6 reacted with this peptide, but the peptide is in a highly variable region.				
gp160 (700–708)	Env (695–705 BH10, LAI)	AVLSVVNRV	HIV-1 infection	human	Maksiutov2002
	• This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is LRIVFAVLSVV) has similarity with the human chemokine-factor 3 fragment LRLVFALVTAV .				
gp160 (700–708)	gp41 (705–714)	AVLSVVNRV	HIV-1 infection	human (A2)	Ferris1999
	• This epitope is processed by a TAP1/2 dependent mechanism				
gp160 (701–720)	gp41 (701–720 BH10)	VLSIVNRVRQGYSPLSFQTH	HIV-1 infection	human (A32)	Safrit1994a
	• Recognized by CTL derived from acute seroconverter				
gp160 (702–721)	Env (702–721)	LSIVNRVRQGYSPLSFQTLT	HIV-1 infection	human	Novitsky2002
	• HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
gp160 (704–712)	gp160 (704–712 LAI)	IVNRNRQGY		human (A*3002)	Brander2001, Goulder2001a
	• C. Brander notes this is an A*3002 epitope				
gp160 (704–712)	gp41	IVNRVRQGY	HIV-1 infection	human (A*3002)	Goulder2001a
	• Epitope name: IY9 (gp41) • HLA-A*3002 is very common in African populations, 50% of Zimbabweans express HLA-A30, 44% in African Zulu, so five new HIV epitopes were characterized that are presented by this HLA molecule • A rapid method was developed combining ELISPOT with intracellular IFN-γ staining of PBMCs to map optimal epitopes, then HLA presenting molecules were defined – this method was completed within 48 to 72 hours of receipt of blood • Two individuals were studied: Subject 199 (HLA A*0201/*3002 B*4402/51 Cw2/5), a Caucasian, and Subject 6007 (HLA A*3002/ B53/*5801 Cw4/7) an African-Caribbean • In both HLA-A*3002 individuals the response to RSLYNTVATLY was dominant • In subject 199 four additional A*3002 epitopes were identified • Three quantitative assays, ELISPOT, precursor frequency and chromium release, confirmed a hierarchy of response: RY11 (p17) > KY9 (gp41) > KY9 (RT-53) > IY9 (gp41)				
gp160 (742–761)	Env (742–761)	RDRSIRLVSGFLALAWDDLR	HIV-1 infection	human	Novitsky2002
	• HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
gp160 (747–755)	gp41 (747–755)	RLVNGSLAL	HIV-1 infection	human (A2)	Parker1992
	• Studied in the context of HLA-A2 peptide binding				
gp160 (747–755)	gp41 (741–749 CM243 subtype CRF01)	RLVSGFLAL	HIV-1 infection	human (A2)	Sriwanthana2001
	• Epitope name: E747-755 • This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand • HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This epitope was reactive in HIV+ control study subject 144 who carried HLA-A2				
gp160 (747–755)	gp41 (741–749 CM243 subtype CRF01)	RLVSGFLAL	HIV-1 infection	human (A2)	Bond2001
	• More than half of a cohort of HIV+ female sex workers (FSW) from Northern Thailand were HLA-A11 positive, and this study concentrated on A11 epitopes in this group, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested. • 2/4 tested FSWs recognized the E clade version of this epitope, which differs from the previously defined B clade version by two amino acids, RLVNGSLAL • This epitope was somewhat conserved 4/8 subtypes: CRF01 (E), B, C, and G				
gp160 (754–768)	gp41	ALIWEDLRSLCLFSY	HIV-1 infection	human (B55)	Jin1998b
	• Progressive HIV-1 infection and CD4 decline was associated decreased the IL-2-expandable HIV-1 CTL response in 10 asymptomatic HIV-infected patients – this observation may be partially due to a reduction and impaired function of T helper cells, CTL exhaustion and APC dysfunction • Continued presence of HIV-1 specific memory cells (CTLp) was observed in three patients, one to GIWGCSGKLICTTAV, one to ALIWEDLRSLCLFSY, and one to PIPIHYCAPAGFAILKCNNK				
gp160 (767–775)	gp41 (766–774 SF2)	SYRRLRDLL	HIV-1 infection	human (A*2402)	Ikeda-Moore1997
	• Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402 • This peptide induced CTL in 1/4 HIV-1+ people tested • SYRRLRDLL bound to A*2402 moderately, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained				
gp160 (767–780)	gp41 (606–614 LAI)	SYHRLRDLLLIVTR	HIV-1 infection	human (A31)	Hammond1995
	• Peptide only processed by a TAP-1/2-dependent pathway • CTL from an acute seroconverter				
gp160 (769–777)	gp41 (769–777 BH10)	HRLRDLLLI	HIV-1 infection	human	Safrit1994a
	• Recognized by CTL derived from acute seroconverter				
gp160 (770–778)	Env (679–777)	RLRDLLLIV	HIV-1 infection	human (A*0201)	Kmieciak1998a
	• CTL responses in six patients to four Env epitopes were studied: D2: LLNATAIAV, 5.3: RLRDLLLIV, D1: KLTPLCVTL, and 4.3: QMHEDIISL – all have A2 anchor residues • The C terminal epitopes (D2 and 5.3) were highly variable and the variability was considered responsible for limited CTL response, while D1 and 4.3, N-terminal epitopes, were much more conserved and gave evidence of high levels of CTL response in vitro • Peptides 5.3 and D2 bound to HLA A*0201 with low affinity.				
gp160 (770–780)	gp41 (775–785)	RLRDLLLIVTR	HIV-1 infection	human	Betts2000
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes • 1/11 of the HLA A2+ was HLA A*0201, A31, B8, B51 and responded to this epitope that has been previously noted to be HLA A3.1, as well as seven others				
gp160 (770–780)	gp41 (768–778 NL43)	RLRDLLLIVTR	HIV-1 infection	human (A*0301)	Takahashi1991
	• CD8+ T cell clone				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (770–780)	gp41 (775–785 LAI)	RLRDLLLIVTR	HIV-1 infection	human (A*0301)	Brander2001
	• C. Brander notes this is an A*0301 epitope				
gp160 (770–780)	gp41 (770–780 BH10)	RLRDLLLIVTR	HIV-1 infection	human (A*3101)	Safrit1994a, Safrit1994b
	• Recognized by CTL derived from acute seroconverter • C. Brander notes that this is an A*3101 epitope in the 1999 database				
gp160 (770–780)	gp160 (770–780 LAI)	RLRDLLLIVTR		human (A*3101)	Brander2001
	• C. Brander notes this is an A*3002 epitope				
gp160 (770–780)	gp41 (768–778 NL43)	RLRDLLLIVTR	HIV-1 infection	human (A3)	Cao1997a
	• The consensus peptide of clade B is RLRDLLLIVTR • The consensus peptide of clades A, C and E is RLRDFILIVTR and it is less reactive • The consensus peptide of clade D is SLRDLLLIVTR and it is less reactive				
gp160 (770–780)	gp41 (775–785)	RLRDLLLIVTR	HIV-1 infection, HIV-1 exposed seronegative	human (A3)	Kaul2001a
	• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers				
gp160 (770–780)	gp41 (770–780)	RLRDLLLIVTR	HIV-1 infection	human (A3)	Day2001
	• The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person • All patients recognized at least 1 A3 epitope, up to 8 A3 epitopes, but none was clearly dominant				
gp160 (770–780)	Nef (73–82)	RLRDLLLIVTR	HIV-1 infection	human (A3)	Day2001
	• The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person • All patients recognized at least 1 A3 epitope, up to 8 A3 epitopes, but none was clearly dominant • In two of the subjects, RLRDLLLIVTR was the dominant epitope				
gp160 (770–780)	gp41 (769–780)	RLRDLLLIVTR	HIV-1 infection	human (A3)	Yu2002a
	• Epitope name: A3-RR11 • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 0/14 HLA-A3 positive individuals had detectable A3-restricted responses to this epitope during acute infection, but only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 1/7 individuals began to have detectable responses to this epitope after STI.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (770–780)	gp41 (770–780)	RLRDLLLIVTR	HIV-1 infection	human (A31)	Ferris1999, Hammond1995
	• This epitope is processed by a TAP1/2 dependent mechanism				
gp160 (777–785)	gp41 (782–790 LAI)	IVTRIVELL		human (A*6802)	Brander2001
	• C. Brander notes this is an A*6802 epitope				
gp160 (781–802)	gp120 (788–809)	IVELLGRRGWEALKYWWNL-LQY	HIV-1 infection	human	Lieberman1995
	• HIV-specific CTL lines developed by ex vivo stimulation with peptide				
gp160 (781–802)	gp41 (788–809 HXB2)	IVELLGRRGWEALKYWWNL-LQY	HIV-1 infection	human (B27)	Lieberman1992
	• CTL epitope defined by T cell line and peptide mapping				
gp160 (786–794)	gp41 (791–799 LAI)	GRRGWEALK	HIV-1 infection	human (B27)	McMichael1994
	• Review of HIV CTL epitopes • Also: J. Liebermann 1992 and pers. comm. J. Liebermann				
gp160 (786–795)	gp41 (791–800 LAI)	GRRGWEALKY	HIV-1 infection	human (B*2705)	Brander2001
	• C. Brander notes this is a B*2705 epitope				
gp160 (786–795)	gp41 (791–800 LAI)	GRRGWEALKY	HIV-1 infection	human (B27)	Lieberman1998
	• Optimal peptide mapped by titration J. Lieberman, Pers. Comm.				
gp160 (786–795)	gp41 (786–795)	GRRGWEALKY	HIV-1 infection	human (B27)	Day2001
gp160 (794–802)	gp160 (794–802 LAI)	KYCWNLLQY		human (A*3002)	Brander2001, Goulder2001a
	• C. Brander notes this is an A*3002 epitope				
gp160 (794–802)	gp41	KYCWNLLQY	HIV-1 infection	human (A*3002)	Goulder2001a
	• Epitope name: KY9 (gp41) • HLA-A*3002 is very common in African populations, 50% of Zimbabweans express HLA-A30, 44% in African Zulu, so five new HIV epitopes were characterized that are presented by this HLA molecule • A rapid method was developed combining ELISPOT with intracellular IFN-γ staining of PBMCs to map optimal epitopes, then HLA presenting molecules were defined – this method was completed within 48 to 72 hours of receipt of blood • Two individuals were studied: Subject 199 (HLA A*0201/*3002 B*4402/51 Cw2/5), a Caucasian, and Subject 6007 (HLA A*3002/ B53/*5801 Cw4/7) an African-Caribbean • In both HLA-A*3002 individuals the response to RSLYNTVATLY was dominant • In subject 199 four additional A*3002 epitopes were identified • Three quantitative assays, ELISPOT, precursor frequency and chromium release, confirmed a hierarchy of response: RY11 (p17) > KY9 (gp41) > KY9 (RT-53) > IY9 (gp41)				
gp160 (794–814)	gp41 (SF2)	KYCWNLLQYWSQELKNSAV-SL	HIV-1 infection	human	Altfeld2000b
	• This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The response to the peptide was CD8 dependent, but the HLA presenting molecule and optimal epitope were not determined				
gp160 (795–816)	gp41 (802–823 HXB2)	YWWNLLQYWSQELKNSAVN-LLN	HIV-1 infection	human	Lieberman1992
	• CTL epitope defined by T cell line and peptide mapping				
gp160 (799–807)	Env (800–808 subtype B)	LLQYWSQEL	Vaccine	human (A2.1)	Kundu1998a
	Vaccine *Vector/Type:* recombinant protein *Strain:* MN *HIV component:* gp160				
	• Ten HIV-1+ HLA A2 asymptomatic individuals were given two courses of HIV-1 MN rgp160 vaccine over a 2 year period				
	• Two hundred and fifty three HIV-1 peptides of 9 or 10 aa possessing the HLA-A2.1 binding motif (Leu at position 2, Val at the C terminus) were identified in gp160, of which 25 had a high or intermediate binding affinity				
	• Eleven peptides were studied that had high HLA-A2 binding affinity – a CTL response was detected to 9/11 peptides in at least 1 individual				
	• CTL responses after reimmunization may include recall responses – only individuals with vaccine cross-reactive sequences prior to vaccination showed detectable CTL responses				
gp160 (805–814)	Env (799–813 BH10, LAI)	QELKNSAVSL	HIV-1 infection	human	Maksiutov2002
	• This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins.				
	• This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is LLQYWSQELKNSAVS) has similarity with the complement component C6 fragment LTQFSSEELKNSGLT.				
	• This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is NSAVSLLNATAIAVA) also has similarity with the human INT-2 proto-oncogene protein precursor (fibroblast growth factor-3) fragment NSAYSILEITAVEVG.				
gp160 (805–814)	gp41 (810–819 LAI)	QELKNSAVSL		human (B*4001)	Brander2001
	• C. Brander notes this is a B*4001,B60 epitope				
gp160 (805–814)	gp41 (SF2)	QELKNSAVSL	HIV-1 infection	human (B60(B*4001))	Altfeld2000b
	• This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes				
	• B60 is present in 10-20% of the Caucasoid and very common in Asian populations				
gp160 (805–814)	gp41 (805–814)	QELKNSAVSL	HIV-1 infection	human (B60/B61)	Day2001
	• No immunodominant responses were detected to five B61-restricted epitopes tested				
	• All five B60-restricted epitopes were reactive in another subject, and the B60-restricted responses together contributed over one-third of the total CTL response				
gp160 (813–822)	gp41 (814–823 LAI)	SLLNATDIAV	Vaccine	human (A*0201)	Dupuis1995
	Vaccine *Vector/Type:* recombinant protein *Strain:* MN *HIV component:* gp160				
	• Of two CTL clones, one reacted only with 815-823, the other with 814-823 and 815-823				
	• Noted to be A*0201 in Brander et al., 1999 database				
gp160 (813–822)	gp41 (818–827 LAI)	SLLNATDIAV	Vaccine	human (A*0201)	Brander2001
	Vaccine *Vector/Type:* recombinant protein *Strain:* MN *HIV component:* gp160				
	• C. Brander notes this is an A*0201 epitope				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (813–822)	gp41 (814–823)	SLLNATDIAV	HIV-1 infection	human (A2)	Kundu1998b
	• Allogeneic dendritic cells (DCs) were obtained from HLA-identical siblings, pulsed with rgp160 MN or A2-restricted HIV-1 epitope peptides, and infused monthly into six HIV-infected patients • 1/6 showed increased env-specific CTL and increased lymphoproliferative responses, 2/6 showed increase only in proliferative responses, and 3/6 showed no change – pulsed DCs were well tolerated • SLLNATDIAV is a conserved HLA-A2 epitope included in this study – 4/6 patients had this sequence as their HIV direct sequence, and 3 of these had a detectable CTL response – the other two had either the sequence SLFNAIDIAV or SLLNTTDIVV and no detectable CTL response • CTL demonstrated against peptide-coated target, epitope is naturally processed and enhancible with vaccine				
gp160 (813–822)	gp41 (818–827)	SLLNATDIAV	HIV-1 infection	human (A2)	Betts2000
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes • 1/11 of the A2+ individuals that didn't respond to SLYNTVATL reacted with seven other epitopes, including this epitope				
gp160 (813–822)	gp41 (SF2)	SLLNATAIAV	HIV-1 infection	human (A2)	Goulder2001a
	• Epitope name: SV10 • Dominant CTL epitope in acute infection of patient AC13– response to this epitope corresponded to reduction of initial viremia • Several other subdominant CTL epitopes were identified in the acute phase, but a response to SL9, SLYNTVATL, was not evident until 18 months post-presentation				
gp160 (813–822)	gp41 (77–85 SF2)	SLLNATDIAV	HIV-1 infection	human (A2)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-A2+ individuals that had a CTL response to this epitope broken down by group: 1/10 group 1, 2/6 group 2, and 1/4 group 3				
gp160 (813–822)	gp41 (814–823 CM243 subtype CRF01)	SLLNATAIAV	HIV-1 infection	human (A2)	Sriwanthana2001
	• Epitope name: E813-82 • This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand • HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed • This epitope was reactive in HIV+ control study subjects 125 and 144 who carried HLA-A2				
gp160 (813–822)	gp41 (814–823 CM243 subtype CRF01)	SLLNATAIAV	HIV-1 infection	human (A2)	Bond2001
	• More than half of a cohort of HIV+ female sex workers (FSW) from Northern Thailand were HLA-A11 positive, and this study concentrated on A11 epitopes in this group, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested. • 1/4 tested FSWs recognized the E clade version of this epitope, which differs from the previously defined B clade version by one amino acid, SLLNATDIAV • This epitope was somewhat conserved 4/8 subtypes: CRF01 (E), B, D, and F				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (813–822)	gp41 (813–822)	SLLNATDIAV	HIV-1 infection	human (A2)	Day2001
	• The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person				
gp160 (813–822)	gp41 (813–822 IIIB)	SLLNATAIAV	Vaccine	murine (A2)	Kiszka2002
	Vaccine *Vector/Type:* DNA, DNA with recombinant protein boost *Strain:* IIIB *HIV component:* gp160, gp160deltaV3 *Adjuvant:* IL-12 (IL-12p35 and IL-12p40) • Epitope name: D2 • Transgenic mice expressing a HLA-A2/Kb chimeric protein were vaccinated with a full length gp160 or with gp160deltaV3, with the V3 loop deleted. Mice given gp160deltaV3 had a broader immune response than those given gp160, with increased responses to conserved HLA-A2 epitopes in the C1 region of gp120, KLTPLCVTL, and the C-term region of gp41, SLLNATAIAV. • Greater resistance was conferred by the gp160deltaV3 than the gp160 vaccine to a challenge of vaccinia expressing heterologous gp160 from primary isolates (VI-06 and 89.6), and the resistance was conferred by CD8+ T-cells.				
gp160 (813–822)	Env (814–823 subtype B)	SLLNATDIAV	Vaccine	human (A2.1)	Kundu1998a
	Vaccine *Vector/Type:* recombinant protein *Strain:* MN *HIV component:* gp160 • Ten HIV-1+ HLA A2 asymptomatic individuals were given two courses of HIV-1 MN rgp160 vaccine over a 2 year period • Two hundred and fifty three HIV-1 peptides of 9 or 10 aa possessing the HLA-A2.1 binding motif (Leu at position 2, Val at the C terminus) were identified in gp160, of which 25 had a high or intermediate binding affinity • Eleven peptides were studied that had high HLA-A2 binding affinity – a CTL response was detected to 9/11 peptides in at least 1 individual • CTL responses after reimmunization may include recall responses – only individuals with vaccine cross-reactive sequences prior to vaccination showed detectable CTL responses • CTL to overlapping peptides in this region gave a positive response in the greatest number of patients • ALTERNATIVE EPITOPES: LLNATDIAV and LLNATDIAVA – CTL were induced by vaccine in those that had the sequence SLLNATAIAVA in their own infection, but not in those with: NLLNTIAIAVA or NLFNTTAIAVA or SLLNATAITVA				
gp160 (813–822)	gp41 (814–823 LAI)	SLLNATDIAV	Vaccine	murine (A2.1)	Peter2001
	Vaccine *Vector/Type:* peptide *Strain:* LAI *Adjuvant:* P30, incomplete Freund's adjuvant (IFA), Montanide (ISA 720), PLG-microparticle • Epitope name: LR27 • The stability of peptide binding to HLA-A2.1 was determined for six HLA-A2.1 peptides included in this vaccine study – ILKEPVHGV (RT), SLYNTVATL (p17), SLLNATDIAV (gp41) and LLWKGEGAV (RT) all bound with high affinity comparable to a influenza epitope reference (GILGFVFTL), while RGPGRAFVTI and VIYQYMDDL bound with a lower affinity (relative binding activity = 0.01). • The four high-affinity peptides formed stable complexes with half-lives ranging between 8 and 32 hours, while the low affinity peptides had half lives of less than an hour. • HLA-A2.1 transgenic mice were immunized with the six HIV-1 peptides and P30, as a universal T-helper epitope, with IFA or Montanide or microspheres as adjuvants. • All peptides except VIYQYMDDL induced a stong CTL response in Cr-release assays - stronger responses were observed when peptides were delivered alone, indicating immunodominance when the combination was used.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (813–822)	gp41 (814–823 LAI)	SLLNATDIAV	Vaccine	murine (A2.1)	Peter2002
	Vaccine *Vector/Type:* peptide *Strain:* LAI *Adjuvant:* P30, incomplete Freund's adjuvant (IFA), IL-12 • Epitope name: LR27 • When HIV-1 peptides were used to vaccinate HLA-A2.1 transgenic A2-Kb mice, strong responses to five peptides were observed when the peptides were given individually, but immunodominance limited the response to some of the peptides when they were given in combination [Peter2001]. IL-12 can counteract immunodominance in BALB/c mice, so it was given with the multiple epitope vaccination, and was instead found to specifically eliminate the HLA-A2.1-epitope CTL responses, but not Kb CTL responses. This was possibly a consequence of transient depletion of T-cells, B cells and macropahges in the spleen.			
gp160 (813–822)	gp41	SLLNATDIAV	HIV-1 infection	human (A68)	Altfeld2001c
	• Epitope name: gp41 SV10 • HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested • Three additional previously described HLA-A2 epitopes were added to the set of 20, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acute infected individuals recognized at least 1 (median of 1 and maximum of 2) • This epitope binds to three HLA-A2 supertype alleles: A*6802 (highest affinity), A*0202 and A*0203 (but not A*0201 and not A*0206) • This epitope did not elicit an ELISPOT response in 22 chronic HIV HLA-A2 infections, but elicited a strong response in 1/12 acute HLA-A2 infections – this individual, AC13, was HLA A*0201/68 B44/14 and also had a strong response to HLA-A2 vpr epitope AIIRILQQL			
gp160 (814–822)	Env (815–823)	LLNATAIAV	HIV-1 infection	human (A*0201)	Kmieciak1998a
	• CTL responses in six patients to four Env epitopes were studied: D2: LLNATAIAV, 5.3: RLRDLLLIV, D1: KLTPLCVTL, and 4.3: QMHEDIISL—all have A2 anchor residues. • The C terminal epitopes (D2 and 5.3) were highly variable and the variability was considered responsible for limited CTL response, while D1 and 4.3, N-terminal epitopes, were much more conserved and gave evidence of high levels of CTL response in vitro. • Peptides 5.3 and D2 bound to HLA A*0201 with low affinity and were variable, particularly D2. • Substitutions in peptide D2: llnTIaiav did not abrogate the response, but diminished it. • In a longitudinal study, the CTL response to the variable D2 epitope diminished over time, while the response to the conserved epitope D1 stayed higher.			
gp160 (814–822)	gp41 (815–823 LAI)	LLNATDIAV	Vaccine	human (A2)	Dupuis1995
	Vaccine *Vector/Type:* recombinant protein *Strain:* MN *HIV component:* gp160 • Of two CTL clones, one reacted only with 815-823, the other with 814-823 and 815-823				
gp160 (814–822)	Env (815–823)	LLNATAIAV	HIV-1 infection	human (A2)	Kmieciak1998b
	• Increased CTL response to cells expressing a VV construct ΔV3 mutant compared with a full-length env gene product				
gp160 (822–832)	gp41 (SF2)	VAEGTDRVIEI	HIV-1 infection	human	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response			

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Number of individuals that had a CTL response to this epitope (HLA presenting molecule uncertain) broken down by group: 0 group 1, 1 group 2, and 0 group 3				
gp160 (827–841)	gp41 (834–848 IIIB)	DRVIEVVQGAYRAIR	HIV-1 exposed seronegative	human	Pinto1995
	• CTL and T helper cell reactivity in healthcare workers exposed to HIV				
gp160 (827–841)	gp41 (834–848 IIIB)	DRVIEVVQGAYRAIR	HIV-1 infection	human (A2)	Clerici1991a
	• Helper and cytotoxic T cells can be stimulated by this peptide (Th4)				
gp160 (827–841)	gp41 (834–848 IIIB)	DRVIEVVQGAYRAIR	Vaccine	murine (H-$2^{d,p,u,q}$)	Shirai1992
	Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* gp160				
	• In a murine system multiple class I molecules can present to CTL				
gp160 (827–841)	gp41 (834–848 IIIB)	DRVIEVVQGAYRAIR	Vaccine	murine (H-$2^{d,p,u,q}$)	Shirai1996b
	Vaccine *Vector/Type:* vaccinia *HIV component:* gp160				
	• Multiple murine MHC can cross-present this epitope (HP53), and P18 RIQRGPGRAFVTIGK, to specific CTL				
gp160 (828–836)	gp41 (829–837 LAI)	RVIEVLQRA	Vaccine	human (A2)	Dupuis1995
	Vaccine *Vector/Type:* recombinant protein *Strain:* MN *HIV component:* gp160				
	• CTL from HLA-A2 positive subject react with this peptide				
gp160 (828–836)	gp41 (829–837 CM243 subtype CRF01)	KVIEVAQGA	HIV-1 infection	human (A2)	Bond2001
	• More than half of a cohort of HIV+ female sex workers (FSW) from Northern Thailand were HLA-A11 positive, and this study concentrated on A11 epitopes in this group, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested.				
	• 1/4 tested FSWs recognized the E clade version of this epitope, which differs from the previously defined B clade version by three amino acids, RvievLqRa				
	• This epitope was only conserved in CRF01 (subtype E), and identities were rare				
gp160 (828–836)	Env (829–837 subtype B)	RVIEVLQRA	Vaccine	human (A2.1)	Kundu1998a
	Vaccine *Vector/Type:* recombinant protein *Strain:* MN *HIV component:* gp160				
	• Ten HIV-1+ HLA A2 asymptomatic individuals were given two courses of HIV-1 MN rgp160 vaccine over a 2 year period				
	• Two hundred and fifty three HIV-1 peptides of 9 or 10 aa possessing the HLA-A2.1 binding motif (Leu at position 2, Val at the C terminus) were identified in gp160, of which 25 had a high or intermediate binding affinity				
	• Eleven peptides were studied that had high HLA-A2 binding affinity – a CTL response was detected to 9/11 peptides in at least 1 individual				
	• CTL responses after reimmunization may include recall responses – individuals with vaccine cross-reactive sequences prior to vaccination showed detectable CTL responses				
gp160 (830–854)	gp41 (831–853)	IEVVQGAYRAIIRHIPRRI-RQGLERI	HIV-1 infection	human	Price1995
	• Study of cytokines released by HIV-1 specific activated CTL				
gp160 (831–838)	Env (830–837)	EVAQRAYR	HIV-1 infection	human (A*3303)	Hossain2001, Takiguchi2000
	• HLA-A33 a very common allele in Asia, with HLA-A*3303 the most common among the Japanese. New A*3303 epitopes were defined to better characterize the immune response in this population.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The anchor motif for HLA*3303 (A, I, L, V, F, Y in position 2 (F and Y bind most strongly), and R (K is also tolerated) in the C-terminal position) was used to define 82 potentially reactive peptides in Env; 37/82 peptides bound to A*3303; 3/37 peptides could induce peptide-specific CTL in bulk PBMC cultures from 1/3 HLA A*3303 positive individuals tested. • 2/3 peptides that reacted with the bulk culture, EVAQRAYR and VIEVAQRAYR, were overlapping, with one encompassing the other, but EVAQRAYR was shown to be the one that was reactive with a CTL clone. • CTL clones were isolated that killed target cells in a concentration dependent manner after pulsing with the EVAQRAYR peptide, that could also kill cells transfected with env expressed from a vaccinia vector. Bulk cultures were tested from six additional people, and only 2/6 reacted with this peptide, but the peptide is in a highly variable region.				
gp160 (835–843)	Env (834–842 SF2)	RAYRAILHI	HIV-1 infection	human (B*5101)	Tomiyama1999
	• HLA-B27, -B51, and -B57 are associated with slow progression to AIDS, while HLA-B35, -B8, -B24 are associated with a rapid progression to AIDS (Nat. Med. 2:405, 1996;Lancet 22:1187, 1986;Hum Immunol 22:73, 1988;Hum Immunol 44:156, 1995) • 15% of Japanese populations carry HLA-B51 while HLA-B27 and -B57 are detected in less than 0.3% • Of the 172 HIV-1 peptides with HLA-B*5101 anchor residues, 33 bound to HLA-B*5101, seven of these peptides were reactive with CTL from 3 B*5101 positive individuals, and six were properly processed • This peptide could stimulate CTL from one person, however this CTL clone did not recognize B*5101 positive target cells infected with HIV-1 recombinant vaccinia expressing Env, so it was not confirmed that this peptide was a properly processed epitope				
gp160 (837–856)	gp120 (844–863)	YRAIRHIPRRIRQGLERILL	HIV-1 infection	human	Lieberman1995
	• HIV-specific CTL lines developed by ex vivo stimulation with peptide				
gp160 (837–856)	gp120 (844–863 SF2)	YRAIRHIPRRIRQGLERILL	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • Eleven subjects had CTL that could recognize vaccinia-expressed LAI gp160 • One of these 11 had CTL response to this peptide • The responding subject was HLA-A2, A26, B7, and B38				
gp160 (837–856)	gp120 (844–863 LAI)	YRAIRHIPRRIRQGLERILL	HIV-1 infection	human (B35)	Shankar1996
gp160 (837–856)	gp41 (844–863 HXB2)	YRAIRHIPRRIRQGLERILL	HIV-1 infection	human (B8)	Lieberman1992
	• CTL epitope defined by T cell line and peptide mapping				
gp160 (842–856)	gp41 (SF2)	HIPRRIRQGLERALL	HIV-1 infection	human	Altfeld2001a
	• HIV+ individual AC-06 was tested for reactive overlapping peptides spanning all HIV-1 proteins in an ELISPOT and was found to react with 12 peptides from 7 proteins, suggesting that the breadth of CTL responses are underestimated if accessory proteins are not included in the study • The only Env peptide recognized was gp41 HIPRRIRQGLERALL				
gp160 (843–851)	gp41 (848–856 LAI)	IPRRIRQGL		human (B*0702)	Brander2001
	• C. Brander notes this is a B*0702 epitope				
gp160 (843–851)	gp41 (848–856 LAI)	IPRRIRQGL		human (B7)	Brander1995b
	• Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study				
gp160 (843–851)		IPRRIRQGL	HIV-1 infection	human (B7)	Soudeyns1999
	• Following primary infection, progressive diversification and accumulation of mutations of HIV-env nucleotide sequences was observed, focused in V2 in one individual and in V8 in another				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The patient with the V2 diversification showed only transient CTL against Env and Nef • The patient with the V8 diversification had an immunodominant CTL response to V8 epitope IPRRIRQGL, and multiple escape variants emerged within a year: ipTrirqgl and ipTrirqgF, which abrogated the CT response in vitro, and also iprrLqgl and iprrirqDl which gave diminished responses.				
gp160 (843–851)	gp41 (848–856 LAI)	IPRRIRQGL	HIV-1 infection	human (B7)	Cao1997a
	• The consensus peptide of clades A, B, D, and F is IPRRIRQGL • The consensus peptide of clade C is iprrirqgF, and it is equally reactive.				
gp160 (843–851)	gp41 (848–856 subtype B)	IPRRIRQGL	HIV-1 infection	human (B7)	Wilson1998b
	• The extent of CTL interclade cross-reactivity from CTL isolated from individuals newly infected with B clade virus was studied, and extensive cross-reactivity was observed • Two HLA B7 individuals had CTL response to B_LAI, A_92UG037 and C_92BR025 gp160, but were B clade strain MN non-responders – the authors note that the B7 epitope IPRRIRQGL is conserved between the LAI and clade A and C strains, but that MN has a non-conservative Arg to Thr substitution at position three that may be contributing to the specificity of the response in the HLA B7 individuals				
gp160 (843–851)	gp41 (843–851 HXB2)	IPRRIRQGL	HIV-1 infection	human (B7)	Hay1999b
	• CTL response to IPRRIRQGL was the immunodominant response in a rapid progressor – there was a subdominant response to SPAIFQSSM in Pol, and interestingly, no response to commonly immunodominant HLA A*0201 epitope SLYNTVATL, although this individual was HLA A*0201 • The individual showed a strong initial CTL response at the time of the initial drop in viremia, but it was quickly lost, although memory cells persisted • Despite the initial narrow response to two epitopes, no other CTL responses developed • No HIV-specific lymphoproliferative responses were detected in this patient, and neutralizing antibody response was weak • Variants were observed in vivo, the most common form of the viral epitope at presentation at 3 months was the only form that did not elicit a CTL response: iprrTrqgl; the other forms detected were iprrirqgF, iprriLqgF, VprrirqgF and they could elicit a CTL response although the response to iprriLqgF was reduced • A second rapid progressor had a detectable CTL response exclusively to this epitope				
gp160 (843–851)	gp41 (subtype A)	IPRRIRQGF	HIV-1 infection	human (B7)	Cao2000
	• HIV-1 subtypes A and D dominate the Ugandan epidemic, and a vaccine trial using B clade antigen is underway – this study addresses relative levels of cross-reactive CTL responses in Ugandans to A, D, and B clade recombinant vaccinia viruses expressing Gag, Env, Pol, RT or Nef from HIV-1 clades A, B, and D • Proteins corresponding to the subtype of the infecting strains tended to trigger higher levels of CTL response measured by percent specific lysis, but there was extensive inter-subtype cross-reactivity with B clade proteins and the co-circulating subtype • This optimal epitope sequence, recognized by CTL derived from a Ugandan with an A subtype infection, is cross-reactive with subtypes A and B, but not in subtype D				
gp160 (843–851)	gp41	IPRRIRQGL	HIV-1 infection	human (B7)	Islam2001
	• Subject 053i was followed longitudinally from acute infection through death, and had rapid progression to AIDS • This individual had a dominant response to IPRRIRQGL with strong in vivo activated responses and in vitro stimulated memory responses and a subdominant response to SPAIFQSSM – during the course of disease progression (4 Years), the functional CTL responses were lost and no sequence variation occurred with in both epitopes • At 3 months post-presentation, seven IPRRIRQGL CTL clones were obtained, five used the T-cell receptor Vbeta 6S1 and Jbeta 2.7 and had the CDR3 WAASS, two used Vbeta16S1, ERSPPGD, Jbeta 2.7 and one CTL clone isolated at 39 months was Vbeta 14S1, CR3 PTAAG, and Jbeta 2.1 – all of these clones persisted over the course of the infection, even to time of death, despite the loss of CTL functional responses over time				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (843–851)	gp41 (843–851 SF2)	IPRRIRQGL	HIV-1 infection	human (B7)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-B7+ individuals that had a CTL response to this epitope broken down by group: 2/4 group 1, 1/3 group 2, and 1/1 group 3			
gp160 (843–851)	gp41 (848–856)	IPRRIRQGL	HIV-1 infection, HIV-1 exposed seronegative	human (B7)	Kaul2001a
	• IPRRIRQGL cross-reacts with clades A, B and D • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure • Among HLA-B7 women, 2/5 HEPS and 5/6 HIV-1 infected women recognized this epitope • The dominant response to this HLA allele was to this epitope in 2 of the 5/6 HIV-1 infected women that responded to the epitope, but in neither of the 2/5 HEPS cases • Subject ML 1203 started with CTL responses to A*6802 DTVLEDINL and to B7 FPVTPQVPLR prior to seroconversion, and upon seroconversion acquired additional responses to A*6802 ETAYFILKL which became dominant, B7 TPGPGV/IRYPL, B7 IPRRIRQGL, and B7 SPRTLNAWV			
gp160 (843–851)	gp41 (843–851)	IPRRIRQGL	HIV-1 infection	human (B7)	Day2001
	• The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person • Subjects with chronic HIV-1 infection recognized between 2-8 out of 11 B7-restricted epitopes • An acute seroconvertor homozygous for the B7 allele recognized five B7-restricted epitopes • The other acute seroconvertor failed to recognize any of the 11 B7-restricted epitopes tested • The B7-restricted CTL response was highly variable and there was no clearly dominant epitope			
gp160 (843–851)	gp41 (SF2)	IPRRIRQGL	HIV-1 infection	human (B7)	Altfeld2000b
	• This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual				
gp160 (843–851)	gp41 (842–852)	IPRRIRQGL	HIV-1 infection	human (B7)	Yu2002a
	• Epitope name: B7-IL9 • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Only two epitopes were detected during acute infection in patient AC-06, B7 restricted gp41 epitope IPRRIRQGL and Gag GPGHKARVL. GPGHKARVL was the first targeted peptide, and remained immunodominant through the 34 month study period. • 6/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. 2/4 individuals had detectable responses to this epitope after STI.				
gp160 (843–851)	gp41	IPRRIRQGL	HIV-1 infection	human (B7)	Altfeld2002
	• Epitope name: B7-IL9(gp41) • Peripheral blood (PB) and lymph node (LN) CD8+ T-cell responses were compared in 15 asymptomatic HIV-1 infected patients using all known optimal CTL epitopes (http://hiv-web.lanl.gov/content/hiv-db/REVIEWS/brander2001.html) for each person's class I HLA alleles. • 60 epitope responses were detected in both PB and LN samples of the 15 patients, and an additional 8 responses were detected only in LN. The total magnitude of the response was similar in LN and PB, but the percentage of CD8+ T cells in the LN is lower so the number of HIV-specific cells per million CD8+ T-cells is higher in the LN. • 1 year post-HAART treatment in five patients studied, the magnitude of the CD8 T-cell response was decreased in both LN and PB, but more dramatically in PB, and 13/25 epitope responses in the PB became undetectable, in contrast to 5/26 in the LN. • Treatment interruption following HAART induced resulted in increased viremia accompanied by the restoration of the detection of 13 epitopes that had become undetectable in the PB, and the addition of 9 novel epitope responses. • Breakdowns of epitope responses were shown for 4 individuals. Patient C displayed the greatest response to B27-KK10(p24), and in decreasing order also responded to A24-RW8(Nef), B7-IL9(gp41), A24-RL9(gp41), A24-YL8(gp41), and B7-TM9(Nef).				
gp160 (845–856)	gp41 (852–863 HXB2)	RRIRQGLERILL	HIV-1 infection	human (A30, B8)	Lieberman1992
	• CTL epitope defined by T cell line and peptide mapping				
gp160 (845–856)	gp41 (852–863 LAI)	RRIRQGLERILL	HIV-1 infection	human (B7)	Shankar1996
gp160 (846–854)		RIRQGLERA	HIV-1 infection	human (A*0205)	Sabbaj2002b
	• Epitope name: Env-RA9 • This study monitored epitope responses in HIV-1 infected minority women living in the United States • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release • This epitope was newly defined in this study • Patient 00RCH28 was African American, not on HAART, had a viral load of 5900 and CD4 count of 889, and she also recognized IN(219-227), KIQNFRVYY, A*3002 • Among HIV+ individuals who carried HLA A02, 6/21 (29%) recognized this epitope				

II-B-19 Env CTL Epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Env	gp160 (LAI, MN)		Vaccine	human	Belshe1998
	Vaccine *Vector/Type:* canarypox prime with rgp120 boost *Strain:* MN, LAI, SF2 *HIV component:* gp120, gp41, Gag, Protease				
	• The live canarypox vaccine ALVAC-HIV(vCP205) carrying MN gp120, LAI gp41, Gag and Protease, and boosted with SF-2 rpg120, was given to HIV-1 seronegative volunteers – HIV-specific Env or Gag CD8+ CTL were detected in 64% of the volunteers				
Env	gp160 (LAV)		HIV-1 infection	human	Zheng1999
	• Protein delivery (gp160 LAV, p66 LAV, and p24 NY5) to human dendritic cells (DC) with liposomes provides enhanced memory CTL response relative to delivery of protein alone				
	• Chloroquine administration enhanced epitope presentation, and brefeldin A and peptide aldehyde inhibitors inhibited antigen presentation, suggesting epitopes were processed by classical proteasome pathway				
Env	Env (IIIB)		HIV-1 infection	human	Wasik2000
	• HIV+ infants that progressed rapidly to AIDS had lower Th1 responses and decreased production of IL-2, as well as beta-chemokines, relative to other HIV+ infants				
	• No HIV+ infants had no demonstrable CTL at birth, but Th1 responses accompanied by CTL responses developed in children with slowly progressive disease, and not in rapid progressors				
	• CTLp frequencies were determined by limiting dilution using autologous B cells infected with vaccina/HIV constructs				
Env	gp120		HIV-1 infection	human	Soudeyns2000
	• Analysis of T cell receptor beta chain variable region repertoire indicates that antiretroviral therapy (ART) and highly active antiretroviral therapy (HAART) decrease global CD8 T cell oligoclonality during primary HIV infection				
	• A sharp decline in HIV-1 gp120-specific CTL clones was observed in HAART-treated subjects				
Env	Env (LAI, MN)		Vaccine	human	Salmon-Ceron1999
	Vaccine *Vector/Type:* canarypox *Strain:* LAI, MN *HIV component:* gp41, Gag, Pro, V3				
	• The vaccine used was a rec canarypox with HIV-1 gp120 MN, tm/gag/protease LAI (vCP205), alone or with p24E-V3 MN synthetic peptide (CLTB-36))				
	• Twenty HIV negative subjects were vaccinated in phase I trial with combinations of vCP205 and CLTB-36				
	• Immunization with vCP205 induced HIV-1-specific ABs to gp120, V3, and p24 antigens, and CTL immune responses against vCP205 were detected after the fourth immunization in 33% of the subjects against Env, Gag and Pol, but the CLTB-36 peptide did not produce AB or CTL immune responses against p24 or gp160				
Env	Env		HIV-1 infection	human	Gamberg1999
	• 13/13 subjects with advanced HIV infections showed CD8 T cell proliferation and differentiation of CTL in vitro, and six individuals showed HIV-specific responses to Gag, Pol, Env or Nef antigens				
	• Data suggests that the functional and genetic integrity of the CD8 T cell repertoire (TCR betaV gene intrafamily genetic diversity) remains intact through advanced HIV infection, although HIV-specific CTL activity decreases				
Env	Env (LAI, MN)		Vaccine	human	Gorse1999b
	Vaccine *Vector/Type:* canarypox prime with rgp120 boost *Strain:* LAI and SF2 *HIV component:* Env, Gag, Pro, Nef, Pro				
	• The vaccine used was rec canarypox expressing HIV-1 env, gag, pol, nef and protease (vCP300) with or without administration of HIV-1 SF-2 rgp120				
	• In vitro inducible CTL activity against HIV-1 Env, Gag, Pol, and Nef antigens was observed in 79% (15 of 19) of vaccine recipients				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The combination of vCP300 and vP1291 together resulted in an overall increase in CTL induction and detection sensitivity				
Env	Env (LAI)		HIV-1 infection	human	Buseyne1998b
	• In infants with positive CTL responses, most responses showed cross-clade reactivity with somewhat diminished recognition of epitopes from different subtypes				
Env	gp120 (IIIB)		Vaccine	Rhesus macaque	Shiver1997
	Vaccine *Vector/Type:* DNA *Strain:* IIIB *HIV component:* gp120, gp160				
	• DNA vaccinations of Rhesus monkeys with a gp120 or gp160 DNA vaccine elicited a strong CD8 cytotoxic T cell response				
Env	gp160		HIV-1 infection	Macaca nemestrina	Kent1997b
	• Macaques can be infected with HIV, and clear the infection within 6 months, so it is of interest to examine their initial immune response				
	• A strong CTL response against env, pol and gag antigens can be detected				
	• The CTL response peaked by 4 weeks and declined dramatically by 8 weeks				
	• The response in the lymph nodes and peripheral blood was comparable				
Env	gp160		Vaccine	murine	Kim1997c
	Vaccine *Vector/Type:* DNA *HIV component:* Gag, Pol, Vif, Env *Adjuvant:* B7, IL-12				
	• A gag/pol, vif or env DNA vaccine, when delivered in conjunction with the plasmid encoding the co-stimulatory molecules B7 and IL-12, gave a dramatic increase in both the cytotoxic and proliferative responses in mice				
	• When IL-12 was present, CTL response could be detected even without in vitro stimulation				
Env	gp160		Vaccine	murine	Kim1997d
	Vaccine *Vector/Type:* DNA *HIV component:* Gag, Pol, Vif, Env *Adjuvant:* B7, IL-12				
	• A gag/pol or env DNA vaccine, when delivered in conjunction with the plasmid encoding the co-stimulatory molecules CD86, gave a dramatic increase in both the cytotoxic and proliferative responses in mice				
	• When CD86 was present, CTL response could be detected even without in vitro stimulation				
Env	gp120 (HXBc2)		Vaccine	Rhesus macaque	Letvin1997
	Vaccine *Vector/Type:* DNA prime with rgp160 boost *Strain:* HXBc2 *HIV component:* gp160				
	• Vaccination of Macaques mulatta (Rhesus monkeys) with an HXBc2 env DNA prime and a protein boost elicited a T cell proliferative response, a CTL response, and type-specific neutralizing antibodies				
	• Vaccinated animals challenged with SHIV-HXB2 were protected from infection				
Env	gp120 (MN)		Vaccine	human	MacGregor1998
	Vaccine *Vector/Type:* DNA *Strain:* MN *HIV component:* Env, Rev				
	• An HIV DNA env and rev vaccine given to 15 asymptomatic HIV+ individuals at three different dosages, 30, 100 or 300 ug, was safe				
	• The CTL response to gp120 was enhanced in 0/4 patients in the 30 μg group, 2/3 patients in the 100 μg group, and 0/3 in the 300 μg group – but the non-responding patients in the 300 μg group had a strong CTL response prior to vaccination, and the CTL results are inconclusive				
Env	gp120 (IIIB)		HIV-1 infection	human	Trickett1998
	• Twelve HIV-1 infected patients were re-infused with their own lymphocytes, cryopreserved from an earlier time point in the infection				
	• Improvement in CD4+ and CD8+ T cells was seen in 7/12, and an increase in the CTL response to Env was seen in one patient				
Env	gp120 (LAI)		HIV-1 infection	human	Legrand1997
	• Seventeen recently infected patients were tested for CTL response to HIV proteins Env, Gag, Pol, Rev, Nef, Vif and Tat				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• An early response (within a month following PI) was noted in 87% of the subjects to Gag, 75% to Env, and 50% to Nef • Early responses to Pol, Rev, Vif and Tat were rare				
Env	gp120 (LAI)		Vaccine	human	Corey1998
	Vaccine *Vector/Type:* vaccinia prime with rgp120 boost *Strain:* LAI, SF2, MN *HIV component:* gp160 • Vaccinia-naive subjects were vaccinated with vaccinia-gp160 LAI and boosted with gp120 SF2, LAI, MN, or 160 MN • 26/51 had an anti-Env CTL response, and those that were boosted with gp120 tended to produce Abs that neutralized autologous laboratory strains with some cross-reactivity				
Env	Env (IIIB)		HIV-1 infection	human	Betts1997
	• 6/8 individuals from Zambia infected with C clade virus had CTL that were able to make response to B clade HIV-1 IIIB vaccinia-expressed Gag, Pol and Env proteins • A vigorous cross-clade response was not limited to a particular protein, and the level of recognition of different proteins varied among the six patients				
Env	Env		HIV-1 infection	human	De Maria1997
	• CD3+ cells that also carry a natural killer cell receptor (NKR+) can exhibit down regulation of T cell function • Anti-NKR IgM MAb masked this inhibitory function and increased HIV-1 specific CTL activity in phytohemagglutinin-activated PBMC cultured in the presence of IL-2 from 3/5 patients, and in one other case anti-NKR MAb brought HIV-1 specific CTL activity to detectable levels				
Env	Env (IIIB)		HIV-1 infection	human	Betts1999
	• This study demonstrated an inverse correlation between HIV Type I plasma viral load and CTL activity directed against HIV-1 Pol, and stronger combined effects of Pol- and Env-specific CTL, in long-term survivors (LTS) of HIV-1 infection				
Env	Env (LAI)		HIV-1 infection	human	Buseyne1998a
	• This study showed a correlation between strong CTL memory and breadth of response in 7-12 month old infants, and remaining AIDS-free for the first year of life, higher absolute CD4 and CD8 cells, and lower viral load				
Env	Env		HIV-1 exposed seronegative	human	Goh1999
	• 13/37 exposed uninfected individuals with repeated high-risk sexual exposure had HIV-1 specific CTL against Env, Gag, Pol, or a combination of proteins – CTL activity was correlated with a CCR5 wildtype genotype • In this group, the highest CTLp frequencies were directed at Gag, but the most common response was to Env and four individuals had responses to multiple HIV-1 proteins				
Env	Env (LAI, MN)		Vaccine	human	Evans1999
	Vaccine *Vector/Type:* canarypox *HIV component:* gp120, gp41, Gag, Pro, Nef, RT • A Canarypox vaccine expressing gp120, gp41, Gag, Protease, Nef and Pol CTL epitopes gave rise to CTL that could be detected in 61% of the volunteers – responses to Gag, Env, Nef and Pol were detected 3-6 months after the last vaccination				
Env	Env (LAI)		Vaccine	Macaca nemestrina	Kent1998
	Vaccine *Vector/Type:* DNA prime with vaccinia boost *Strain:* LAI *HIV component:* Env, Gag • Priming with an HIV-DNA vaccine and boosting with a vaccinia construct induced greater levels of HIV T cell immunity than either vaccine alone • The proliferative response to Env and Gag after the DNA vaccination had a mean SI of 1.5-4, but after boosting with rHIV-fowlpox virus, there was a 6-17 fold increase in the mean SI for HIV Gag and Env. The T help response happened despite a fall in antibody titers, suggesting that the Th response was primarily Th1, not Th2. The CTL response was also enhanced				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Env	Env (LAI, MN)		Vaccine	human	Salmon-Ceron1999
	Vaccine *Vector/Type:* canarypox *Strain:* MN, LAI *HIV component:* gp120, gp41, Gag, Protease				
	• A live attenuated canarypox vector expressing MN gp120 and LAI gp41/gag/protease could induce CTL and a lymphoproliferative response in healthy, uninfected volunteers				
Env	Env (MN)		Vaccine	chimpanzee	Kim1998
	Vaccine *Vector/Type:* DNA *HIV component:* Env, Gag, Pol *Adjuvant:* CD86, CD80				
	• The study explores the use of co-stimulatory molecules co-expressed with an HIV-1 immunogen in a DNA vaccine to enhance the immune response – co-expression of CD86, but not CD80, dramatically increased both HIV Env and Gag/Pol specific CTL and Th proliferative responses				
Env	gp120 (IIIB)		Vaccine	Rhesus macaque	Notka1999
	Vaccine *Vector/Type:* Semliki-Forest Virus with virus-like particle boost *Strain:* IIIB *HIV component:* gag, gp120				
	• Immunization of SIV Pr56Gag-derived VLPs with HIV-1 gp120 anchored on their surface induced Abs, CTL and Th responses to HIV gp120; priming with the HIV antigens in Semliki-Forest Viruses enhanced the immunological outcome				
	• Immunized monkeys challenged with SHIV showed a more rapid reduction of plasma viremia				
Env	Env		HIV-1 exposed seronegative	human	Akridge1999
	• This study suggests that HIV-1-resistance in exposed and uninfected individuals is not only associated with the 32-bp deletion in the HIV-1 co-receptor CCR5, but can be related to HIV-1 specific CTL immunity				
Env	gp120 (BRU)		HIV-1 infection	human	Aladdin1999
	• In vitro measurements of CTL-activity by Cr release assay in bulk culture showed no correlation between CTL-activity (gp120, Gag, Pol and Nef) and disease progression as measured by viral load, CD4 and time to death				
Env	gp120		HIV-1 infection	human	Aladdin2000
	• The administration of IL-2 caused an initial enhancement of CD4 cell counts that was accompanied by a decrease in CTL activity – IL-2 therapy did not reduce initial HIV viral load and viral replication was ultimately enhanced				
Env	Env		HIV-1 infection	human	Jin1998a
	• CTL precursor frequencies were determined in HIV-1 infected pregnant women, and higher CTLp frequencies to Pol and SF2 Nef, but not IIIB Nef, were found in non-transmitting mothers than in transmitting mothers – Nef CTL responses have been found in uninfected infants born to HIV+ women (Lazuriaga95);				
	• Very different CTLp frequencies were observed in env depending on whether IIIB, MN, RF, BK, or SF2 was used as antigen – no association between env specific CTL and transmission was observed				
Env	Env		Vaccine		Zavala2001
	Vaccine *Vector/Type:* vaccinia *HIV component:* Env				
	• This paper is a review of vaccinia in the context of vaccines strategies that use different vectors to prime and boost, and emphasizes a unique capacity of vaccinia to very efficiently boost memory T-cell responses				
	• HIV is discussed in the context of Gonazalo et al. 1999, where a V3 CTL epitope expressed in reFlu was boosted most effectively by vaccinia expressing the full Env				
Env	Env		Vaccine	Rhesus macaque	Akahata2000
	Vaccine *Vector/Type:* DNA *Strain:* ZF1 *HIV component:* complete genome				
	• Rhesus macaques were vaccinated by i.m. injection with naked plasmid DNA carrying an HIV-1 complete genome vaccine, strain ZF1, with a mutated zinc finger in the nucleocapsid to prevent packaging				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Env and Gag specific CTL but no antibody responses were induced in 2/4 vaccinated monkeys (MM145 and MM153) • 2/4 monkeys (MM146 and MM143) produced antibodies against p24 and/or gp160, but no CTL response was detected • PBMC from all vaccinated monkeys produced IFN-gamma, in response to HIV-1 gp160, indicating a Th response – this response was 5 times higher in MM145, the animal with the strongest CTL response • 4 weeks post-challenge with SHIV NM-3rN plasma viral loads of both MM145 and MM153 (with a homologous Env) decreased to near or below the detection limit • 6-8 weeks post-challenge with SHIV NM-3rN plasma viral loads of both MM146 and MM143 decreased near or below the detection limit				
Env	gp120		HIV-1 infection	human	Young2001
	• Addition of recombinant rec human IL12 (rhIL12) to cultures increased HIV-specific lysis of HIV-Gag, Pol and gp120 vaccinia expressed antigens (11/15 tested increased lysis by > 5%) if the culture was derived from HIV+ individuals who had CD4 cells/ul > 500 • 2/10 individuals with <200 CD4 cells/ul, and 3/10 individuals with 200-500 CD4cells/ul, had an increase of >5% upon treatment of the culture with rhIL12, so a few individuals in late stage disease had CD8 cells that maintained responsiveness to rhIL12				
Env	Env (subtype A, B, D)		HIV-1 infection	human	Cao2000
	• HIV-1 subtypes A and D dominate the Ugandan epidemic, and a vaccine trial using B clade antigen is underway – this study addresses relative levels of cross-reactive CTL responses in HIV infected Ugandans to A, D, and B clade recombinant vaccinia viruses expressing Gag, Env, Pol, RT or Nef from HIV-1 clades A, B, and D • Proteins corresponding to the subtype of the infecting strains tended to trigger higher levels of CTL response measured by percent specific lysis, but there was extensive inter-subtype cross-reactivity with B clade proteins and the co-circulating subtype				
Env	Env		Vaccine	human	AVEG022PT2001
	Vaccine *Vector/Type:* canarypox, recombinant protein *Strain:* MN (gp120), LAI (gp120, protease and gag), and SF2 gp120 *HIV component:* Env, Gag, Protease *Adjuvant:* MF-59 adjuvant • 26/42 subjects who received CP vac-env-pro vaccine had a CTL response measured by Cr-release, while only 3/17 who were vaccinated with rec gp120 had a CTL response • A combination of a CP vac-env-pro vaccine with rec gp120 gave CD8+ T-cells in 62% of subjects, and NAbs in 91% of subjects				
Env	Env		HIV-1 infection	human	White2001
	• HIV-specific CTL activity was detected in the female reproductive tract of only 1/3 HIV-infected women who underwent a hysterectomy, although CTL could be identified in the PBMC of all three women				
Env	Env (IIIB)		HIV-1 infection	human	Jin2000a
	• The CTL precursor level (CTLp) was measured in long term non-progressors (LTNP) with low viral load using limiting dilution analysis and measuring CTL against Env Gag and Pol expressed in vaccinia in autologous targets • LTNPs have high memory CTL numbers and low viral load				
Env	Env (IIIB)		HIV-1 infection	human	Jin2000a
	• The CTL effector levels (CTLe) were compared in long term non-progressors (LTNP) with low viral load and in patients whose virus was well-suppressed by therapy, using a tetramer assay • LTNPs have high memory CTLe numbers and low viral load, while HAART patients had low CTLe numbers and low viral load				
Env	Env		HIV-1 exposed seronegative	human	Rowland-Jones2001
	• This is a review that summarizes observations about HIV-specific CTL found in the HIV-1 exposed persistently seronegative (HEPS) population				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The CTL responses assayed by ELISPOT and by CTL precursor frequencies by limiting dilution analysis indicate that CTL in HEPS individuals tend to be of a lower magnitude than in chronic HIV-1 infections – the responses in HEPS cases are below the level of detection by tetramer assays • CD8+ CTL responses tend to be detectable in HEPS subjects only if they are recently exposed, and the response diminishes if exposure is reduced – it is not clear if there is a stable memory population in HEPS cases • CD8+ CTL responses in the HEPS population are associated with HIV-1 specific CD4+ T cell responses, assayed by proliferation assays, IL-2 secretion, and ELISPOT, and the authors consider the possibility that HIV-1-specific T-help responses improve the "quality" of the CD8+ response in HEPS individuals relative to HIV-1 infected individuals, who tend to have a poor HIV-1-specific T-help response • HIV-1 specific CD8+ CTL responses in HIV-1 infected individuals show reduced levels of perforin, and the T cells may not mature properly, and although similar studies have not been conducted in HEPS individuals this is considered as a possible difference in the CTL immune response in HEPS and HIV-1 infected people			
Env			Vaccine	murine	Nabel2002
	Vaccine *Vector/Type:* DNA *HIV component:* Gag, Pol, Env • Env DNA constructs were designed that were codon optimized for human genes, express Env in the absence of the regulatory protein Rev, both increasing Env expression levels, deletions in the cleavage site and in the fusion domain. These constructs increased Ab responses to Env, while not diminishing CTL responses, when injected into mice. • Removing N-linked glycosylation sites did not alter the humoral or cellular immune responses to this HIV protein, as has been seen in analogous SIV experiments.				
Env			HIV-1 exposed seronegative	human	De Maria1994, Kuhn2002
	• 6/24 HIV uninfected infants (ages 15-50 months) born to HIV+ mothers had HIV-1 specific CTL responses to vaccinia-expressed Nef, Gag/Pol, Env. • Reviewed in [Kuhn2002].				
Env			HIV-1 infection	human	Kuhn2002, Wasik1999
	• In HIV-infected infants HIV-specific, CTL responses were not detectable in cord blood or in PBMC collected shortly after birth and were absent or remained very low in 3 infants with a rapidly progressive disease. For those who progressed more slowly, the HIV-specific CTL activity varied. • The two infants with high levels of Env peptide-stimulated IL-2 responses had the highest CTLp frequencies. • Stronger responses were detected after initiation of the antiretroviral therapy. • Two babies that were not infected though born to HIV+ mothers had detectable though low HIV-specific CTLp responses to Env (1/2), Pol (2/2), Gag (1/2) cord blood and transiently in PBMC after birth. • Reviewed in [Kuhn2002].				
Env			HIV-1 infection	human	Aldhous1994, Kuhn2002
	• Six of nine HIV vertically infected infants had HIV-1 specific CTL responses to vaccinia expressed Tat (4/6), Pol (6/6), Env (1/6), or Gag (1/6), but not all responses were detected at all time points. • Two of eleven babies that were not infected though born to HIV+ mothers had detectable responses Tat (1/2), Pol (2/2), Gag (1/2). • Reviewed in [Kuhn2002].				
Env			HIV-1 infection	human	Kuhn2002, McFarland1994
	• Only 9% of HIV+ infants had HIV-specific CTL against Env or Gag in unstimulated PBMC. After CD3 stimulation of PBMC, Gag and Env specific CTL were found in PBMC from 91% and 78% of HIV-infected children, respectively, with high precursor frequencies. • 2/9 babies that were not infected though born to HIV+ mothers had detectable responses to Env. • Reviewed in [Kuhn2002].				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Env			HIV-1 infection	human	Yusim2002
• Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17. • While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins. • In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed.					
Env			HIV-1 infection	human	Trabattoni2002
• CD8+ T-cells that were stimulated by HIV-1 Env expressing targets from 25 HIV+ patients receiving ART and 17 ART-naive patients were compared. CTL from the individuals receiving ART showed increased TNFalpha production and a reduction of perforin and granzyme expressing CTL, suggesting a functional defect in ART-treated individuals, and a potential benefit of immunomodulants during therapy.					
Env	(HXB2)		HIV-1 infection	human	Edwards2002
• 96% (26/27) chronically infected HIV-1 infected patients elicited gamma-IFN CD8+ T-cell responses against Gag • Nef and/or Pol CTL responses were detected in 86% of the subjects • The magnitude and breadth of Gag and p24 T-cell responses correlated with absolute CD4 counts, and inversely correlated with viral load • Pol and Int CTL responses correlated positively with absolute CD4+ T-cell count • Nef and Env responses did not correlate with either CD4 counts or viral load					
Env	Env		Vaccine	murine	Ishii2001
Vaccine *Vector/Type:* DNA *Strain:* IIIB *HIV component:* gp160, Rev *Adjuvant:* cationic liposome, IL2, GMCSF • Vaccination route of HIV-1 DNA immunization with gp160 and Rev genes was compared including intranasal (i.n.), intramuscular (i.m.), and topical application of DNA directly on the skin after elimination of keratinocyte layers using a strong adhesive. Topical exposure resulted in high level CTL responses, IFN-gamma and IL-4 production, and delayed type hypersensitivity (DTH). Topical application favored Th2 responses. • DNA delivered topically with adjuvant-like cationic liposomes gave a stronger response than DNA alone, and co-administration of the DNA vaccine with IL-12 and GM-CSF expression vectors enhanced cytotoxic activity and DTH.					
Env			HIV-1 infection	human	Larsson2002b
• Autologous mature dendritic cells with rec vaccinia expressing Gag, Pol, Nef and Env could amplify CD8+ T-cell Elispot responses 4-38 fold in five HIV+ patients on successful HAART treatment, relative to autologous monocytes. Some weak responses could only be detected using mature dendritic cells as APCs, and this approach could be useful for detection of low frequency memory cells.					
Env	(IIIB)		HIV-1 infection	human	Trickett2002
• Conditions were optimized for ex-vivo expansion of CD8+ and CD4+ T-cells with the goal of functional T-cell production for autologous immunotherapy. 10,000-fold expansions were obtained in 14 days with optimized concentrations of IL-2, anti-CD3 and anti-CD28 coated microspheres, and decreasing amounts of serum over the first 8 days.					
Env	(IIIB)		HIV-1 and HCV co-infection	human	Lauer2002
• HIV-1 and HCV immune responses were studied in 22 individuals who were co-infected with HIV-1 and hepatitis C virus (HCV). IFNgamma production was measured in an Elispot assay of CD8+ T-cells using targets expressing either Gag, RT, Env and Nef in a vaccinia construct, or one of seven HCV proteins.					

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• All 22 patients targeted at least one protein. 20/22 patients recognized RT, 17/22 patients recognized Gag, 13/22 subjects recognized Env and 11/22 patients recognized Nef. Robust CTL activity was independent of disease progression or viral load. • Despite high HCV viral loads, very few HCV CD8+ T-cell Elispot responses were detected. In a control HCV infected person who did not have HIV-1, strong anti-HCV responses were mounted. • HIV-specific CD4 proliferative responses were detected in 9/17 coinfected patients, but no HCV responses were detected.				
Env			HIV-1 infection	human	Luzuriaga1995
	• 2/3 infants infected in utero had detectable HIV-1 Gag and Env specific CTL responses, one by 4 months, one by 11 months of age. Levels of the responses varied at different time point. Pol responses were not detected. • 2/4 infants infected intrapartum had detectable responses, one note until 11 months, one not until 42 months. • HIV-specific CTL were not detected in ten HIV- infants that were born to HIV+ mothers.				
Env			Vaccine	human	Gupta2002
	Vaccine *Vector/Type:* canarypox prime with rgp120 boost *HIV component:* gag, env *Adjuvant:* Gag, LAI; gp120, MN; and gp41, LAI • A safety and immunogeniticity study of a vaccine dosing schedule was studied in a trial conducted in high and low risk study subjects. There was a 76% cumulative probability of detecting a Gag or Env CTL response by day 728.				
Env			HIV-1 infection	human	Scott2001
	• CTL responses before and after initiation of ART were studied in 13 HIV-1 vertically infected infants <6 months of age, and 4 that were >6 months of age. • Before ART 2/13 infants <6 months of age showed IFNgamma Elispot CD8+ T-cell responses, one to Nef and one to Env and Nef, and these responses became undetectable after successful therapy– 3 infants were coinfected with CMV and all 3 had CMV-specific CD8+ T-cell responses. • One older infant, at 23 months, had CTL responses against all for proteins tested, Gag, Pol, Nef and Env, and had the lowest plasma viremia of the study group. 3/4 infants older than 6 months of age responded to either Nef or Pol. • Administration of ART over 48 weeks broadened the HIV-1-specific CTL response in 2/4 of the older children that were incomplete responders.				
Env	(IIIB)		HIV-1 infection	human	Ortiz2001
	• Immune responses in eight chronically HIV-1 infected patients undergoing HAART therapy structured treatment interruptions (STI) were studied. STI boosted HIV-1 specific CTL responses and elevated CTL responses were maintained up to 22 weeks after the last treatment interruption, but viral load rebound to pretreatment levels and CD4 T-cell count decline was observed. CD8 responses in PBMC were measured by cytokine flow cytometry with gp160, Gag p55, RT-Pol and Nef expressed in vaccinia. • One of seven subjects with a detectable NAb response had an augmented neutralization titer in response to STI.				
Env	(SF2)		HIV-1 infection	human	Tomiyama2002
	• Nef down-regulates class I molecules, and the killing activity of HLA B*3501, A*2402, B*5101 and B*3303-restricted HIV-1-epitope specific CTL clones was inhibited by an HIV-1 strain carrying Nef, relative to a Nef-deleted virus; while Nef-induced HLA class I down-regulation inhibited lysis, it did not abolish cytokine production by HIV-1-specific CD8+ T-cells.				
Env			computer prediction	(A*0201, B*3501)	Schönbach2002
	• Computational methods (artificial neural networks, hidden Markov models, binding matrices based on HLA association rates) were used to identify HLA-A*0201 and HLA-B*3501 HIV T-cell epitope candidates from 533 Gag, Env and Pol sequences of which 374 were derived from HIV-1, 97 were derived from HIV-2 and 62 from SIV. Comparisons to known epitopes and between clades were made.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Env			Vaccine	human (A1, A2, A24, B62, A25, A26, A30, A31, B8, B17, B39, B51, B57, B60, B62, B70)	Ferrari2001
	Vaccine *Vector/Type:* canarypox prime with rgp120 boost, canarypox prime with rgp160 boost *Strain:* gp41 LAI, Gag LAI, gp120 MN, gp120 SF2 *HIV component:* gp120, gp41, Gag, Pol and Nef epitope rich regions				
	• HLA-B62 responses dominated the responses against an Env vaccine in an individual (022JAV) who was HLA A2, A26, B35, B62. The strongest response was against the MN peptide 381-400; a response diminished by half was observed against vaccinia expressed clade A and clade C relative to clade B.				
	• Class I presentation of Env CTL responses in vaccinee 022A12K: A25 > B39, A1 and B8 were undetectable.				
	• Class I presentation of Env CTL responses in vaccinee 022A12N: B57 » A2 > A26 and B60.				
	• Class I presentation of Env CTL responses in vaccinee 034GP3: A31 > A24 > B62 > B51.				
	• Class I presentation of Env CTL responses in vaccinee 0348PP: B17 > B70, A1 and A30 were undetectable.				
Env	gp120 (303–327)		HIV-1 infection	human (A2, A3, A11, B27)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
	• For this cluster of epitopes spanning the tip of the V3 loop, they suggest including a sequence from each clade				
Env			Vaccine	human (A2, B8)	Ferrari2001
	Vaccine *Vector/Type:* canarypox prime with rgp120 boost, canarypox prime with rgp160 boost *Strain:* gp41 LAI, Gag LAI, gp120 MN, gp120 SF2 *HIV component:* gp120, gp41, Gag, Pol and Nef epitope rich regions				
	• No HLA-A*0201 or B8 responses were made against the Env vaccine in individuals carrying these alleles, despite these being common presenting molecules for CTL responses to natural infections.				
Env	Env		HIV-1 infection	human (B*35)	Jin2002
	• Patients with HLA-B*35 variants B*3502, B*3503, B*3504, and B*5301 tend to proceed to AIDS more quickly than those with B*3501.				
	• Of 32 patients with HLA-B*35 alleles CD8+ CTL responses were quantified using an intracellular cytokine staining assay – 75% had responses to Pol, 69% to Gag, 50% to Nef, and 41% to Env.				
	• The overall magnitude of CTL responses did not differ between those bearing B*3501 and the others. A higher percentage of Gag responses was observed in those that had lower RNA levels that carried B*3501, and there was a negative association with viral load and CTL activity. The data is consistent with higher levels of CTL responses contributing to protection in B*3501 individuals, but not in B*3502, B*3503, B*3504, and B*5301 individuals.				
Env	gp41 (842–850 IIIB, BH8)		HIV-1 infection	human (B7)	Pantaleo1997, Soudeyns1997
	• Clonotype-specific PCR and analysis of in vivo HIV-specific CTL showed that in early infection HIV-specific CTL clones preferentially accumulate in blood rather than lymph nodes and that they accumulate prior to down-regulation of virus				
Env	gp160 (MN)		Vaccine	murine (H-2^d)	Vinner1999
	Vaccine *Vector/Type:* DNA *Strain:* MN *HIV component:* gp160, gp120, codon-optimized				
	• Mammalian codon optimization renders gp160 expression Rev independent, increases gp160 expression levels, and DNA vaccination of BALB/c mice yields a higher antibody response with an earlier onset than wild type				
	• Secreted gp120 gave higher antibody titers than membrane bound gp160				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• In contrast to antibodies, synthetic codon-optimized DNA did not alter the CTL response, wild type genes generated equally strong CTL responses				
Env	(IIIB)		Vaccine	murine (H-2^d)	Kato2000
	Vaccine *Vector/Type:* peptide *HIV component:* V3 *Adjuvant:* Cholera Toxin adjuvant, IL-4, GMCSF • A multicomponent peptide vaccine VC1 with cholera toxin adjuvant was given to mice. • Immunization of BALB/c mice with VC1 and CT induced a strong CTL response which was enhanced by IL-12 expressing plasmids • Immunization with VC1 and CT resulted in HIV-1 specific IgA antibody responses, which were increased by the combination of IL-4 or GM-CSF expressing plasmids				
Env	gp160 (IIIB)		Vaccine	murine (H-2^d)	Kaneko2000
	Vaccine *Vector/Type:* DNA *Strain:* IIIB *HIV component:* gp160 *Adjuvant:* PLG-microparticle • A PLG-microparticle encapsulated DNA encoding gp160 was given to mice. • Oral DNA vaccination of BALB/c mice induced mucosal and systemic gp160 glycoprotein-specific cellular and humoral immune responses, and mice vaccinated orally had higher resistance to HIV-env expressing vaccinia intrarectal challenge than mice vaccinated i.m.				
Env	Env		Vaccine	murine (H-2^d)	Ishii1997
	Vaccine *Vector/Type:* DNA with CMV promotor with cationic liposome *HIV component:* gp160, Rev • pCMV160/Rev is a DNA vaccine candidate carrying gp160 and Rev linked to a cytomegalovirus (CMV promotor)				
Env	Env		Vaccine	murine (H-2^d)	Xin2001
	Vaccine *Vector/Type:* adeno-associated virus (AAV) *HIV component:* Env, Tat, Rev *Adjuvant:* IL2 • An AAV vector expressing HIV-1 env, tat, and rev genes (AAV-HIV vector) was used to vaccinate BALB/c mice • A single injection stimulated and long lasting serum IgG, fecal IgA, and HIV-specific CTL • Boosting enhanced the humoral response, and IL2 enhanced T-cell immunity				
Env	Env		Vaccine	murine (H-2^d)	Gonzalo1999
	Vaccine *Vector/Type:* influenza, vaccinia *Strain:* IIIB *HIV component:* V3, Env • The use of two different live vectors for priming and boosting has a synergistic effect on the immune response against HIV-1 – a 5-6 fold enhanced CTL response in Balb/c mice occurred when they were immunized with rec influenza virus (Flu-Env) expressing the V3 loop epitope from HIV-1 strain IIIB, and boosted with a vaccinia virus recombinant (VV-Env) expressing the complete HIV-1-IIIB env protein, comared to either immunogen alone				
Env	Env (subtype B)		Vaccine	murine (H-2^d)	McGettigan2001
	Vaccine *Vector/Type:* rabies virus *Strain:* NL4-3, 89.6 *HIV component:* gp160 • BALB/c were immunized with a replication competent recombinant rabies virus (RV) vaccine expressing HIV-1 gp160 • A single vaccination induced induced strong and long-lasting (4.5 months) gp160-specific CTL cytotoxic responses • Although the greatest specific lysis was achieved when the vaccine strain was also used as the in vitro the target strain to assess the response, there was extensive CTL cross-reactivity against other B clade HIV-1 envelope proteins, implying CTL recognition of multiple epitopes within the HIV-1 envelope protein				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Env	Env (SIV)		SIV infection	Rhesus macaque (Mamu-A*11, -B*03, -B*04, and -B*17)	Dzuris2000
	• Cell binding assays for Mamu molecules were employed to describe the peptide binding motifs for Mamu-A*11, -B*03, -B*03, -B*04, and -B*17 CTL epitopes – a similarity for Mamu-A*11 and -B*03 and human HLA-B*44 and -B*27, respectively, was observed – all epitopes studied were SIV epitopes, so not specifically listed here				

II-B-20 Nef CTL Epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (1–16)	Nef (1–16)	MGGKWSKSSIVGWPAV	HIV-1 infection	human	Novitsky2002
	• HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
Nef (13–20)	Nef (13–20 LAI)	WPTVRERM	HIV-1 infection	human (B*0801)	Brander2001, Goulder1997g
	• C. Brander notes this is a B*0801 epitope				
Nef (13–20)	Nef (HXB2)	WPTVRERM	HIV-1 infection	(B*0801)	Peng2001
	• Deletion of the 19 N-terminal amino acids from Nef including the myristolation signal eliminates Nef-induced down-regulation of MHC class I and CD4 molecules. Such a construct has the potential to serve as a more potent immunogen. The known T-cell epitopes that that would be disputed by this deletion are minimal, including the HLA-B8 CTL epitope WPTVRERM.				
Nef (13–20)	Nef (13–20 LAI)	WPTVRERM	HIV-1 infection	human (B8)	Goulder1997g
	• Unusual epitope for HLA-B8, but compatible with crystal structure predictions				
Nef (13–20)	Nef (13–20)	WPTVRERM	HIV-1 infection	human (B8)	Betts2000
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes • 1/11 of the HLA A2+ was HLA A*0201, A31, B8, B51 and responded to this epitope as well as seven others				
Nef (13–20)	Nef (13–20 SF2)	WPTVRERM	HIV-1 infection	human (B8)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-B8+ individuals that had a CTL response to this epitope broken down by group: 1/3 group 1, 0/3 group 2, and 1/2 group 3				
Nef (13–20)	Nef (13–20)	WPTVRERM	HIV-1 infection	human (B8)	Day2001
	• B8-restricted CTL accounted for about 1/3 of the total CTL response in one individual				
Nef (42–50)	Nef (44–52 HXB3)	ALTSSNTAA	Vaccine	murine (HLA-A201 transgenic)	Sandberg2000
	Vaccine *Vector/Type:* DNA, peptide *Strain:* HXB3 *HIV component:* Nef *Adjuvant:* Freund's adjuvant • Ten Nef 9-mer peptides were predicted to have a strong binding affinity with HLA-A*0201 – of these, four did bind strongly by a T2 class I stabilization assay, several others bound weakly • A CTL immune response to only 3/10 peptides was detected by a 51Cr-release assay after immunization of HLA-A201 transgenic mice with either nef DNA under the control of a CMV promotor, coated on gold particles delivered to abdominal skin by gene gun • ALTSSNTAA was also tested by subcutaneous injection of Nef peptides in Freund's adjuvant				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• ALTSSNTAA bound weakly to HLA-A2, but it had the strongest CTL response among the three elicited by the DNA vaccine and a strong response to the peptide vaccination				
Nef (48–56)	Nef (58–66 JRFL)	TAATNADCA	Vaccine	murine (H-2^b)	Liang2002
	Vaccine *Vector/Type:* DNA *Strain:* JRFL				
	• BALB/c, C3H/HeN and C57BL/6 mice were given intramuscular immunization with Nef DNA constructs – C57BL/6 responded to this epitope.				
	• The Nef mutant that lacked the myristylation site (G–>A) at position 2, and the dileucine motif (L –> A at positions 174 and 175) was impaired in terms of its ability to elicit induction of Nef-specific CD4+ and CD8+ T-cell responses. The myristylation site is critical for Nef membrane localization and function, and the di-leucine motif for the down-regulation of surface CD4 molecules, and the mutation of these regions could yield a safer vaccine.				
	• N-terminal addition of human tissue plasminogen activator (TPA) to Nef, enhanced CD8+ T-cell responses and could compensate for the G2A, L174A, L175A mutations – this enhanced immunogenicity correlated with enhanced levels of protein expression in transfected cells.				
Nef (62–81)	Nef (61–80)	EEEEVGFPVTPQVPLRPMTY	HIV-1 infection	human	Lieberman1995
	• HIV-specific CTL lines developed by ex vivo stimulation with peptide				
Nef (62–81)	Nef (61–80 SF2)	EEEEVGFPVTPQVPLRPMTY	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein				
	• Twelve subjects had CTL that could recognize vaccinia-expressed LAI Nef				
	• Two of these 12 had CTL response to this peptide				
	• The responding subjects were HLA-A11, A24, B8, B35, and HLA not determined				
Nef (62–81)	Nef (61–80 SF2)	EEEEVGFVTPQVPLRPMTY	HIV-1 infection	human	Lieberman1997b
	• CTL expanded ex vivo were later infused into HIV-1 infected patients				
Nef (62–81)	Nef (SF2)	EEEEVGFPVTPQVPLRPMTY	HIV-1 infection	human	Altfeld2001a
	• HIV+ individual AC-06 was tested for reactive overlapping peptides spanning all HIV-1 proteins in an ELISPOT and was found to react with 12 peptides from 7 proteins, suggesting that the breadth of CTL responses are underestimated if accessory proteins are not included in the study				
	• Nef peptides PQVPLRRMTYKAAVDLSHFL, KAAVDLSHFLKEKGGLEGLI and EEEEVGFPVTPQVPLRPMTY were recognized and the first two share KAAVDLSHFL (a Cw8 epitope), the first and last share PQVPLRPMTY				
Nef (66–80)	Nef (66–80 BRU)	VGFPVTPQVPLRMT	HIV-1 infection	human (A1, B8)	Hadida1992
	• HIV-1 specific CTLs detected in lymphoid organs of HIV-1 infected patients				
Nef (66–80)	Nef (64–78)	VGFPVTPQVPLRMT	HIV-1 infection	human (A1, B8)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
Nef (66–97)	Nef (66–97 LAI)	VGFPVTPQVPLRPMTYKAA-VDLSHFLKEKGGL	Vaccine	human	Gahery-Segard2000
	Vaccine *Vector/Type:* lipopeptide *HIV component:* six peptides				
	• Anti-HIV lipopeptide vaccine consisting of six long amino acid peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial				
	• A CD4+ T cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 5/10 reacted to this Nef peptide				
	• 9/12 tested mounted a CTL response to at least one of the six peptides; each of the six peptides elicited a CTL response in at least one individual				
	• 5/12 tested had an IgG response to this peptide				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (67–81)	Nef (67–81)	GFPVRPQVPLRPMTY	HIV-1 infection	human	Novitsky2002
	• HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
Nef (68–76)	Nef (72–80 SF2)	FPVRPQVPL	HIV-1 infection	human (B*3501)	Tomiyama1997
	• A CTL clone responsive to this epitope was obtained • 3/7 B35-positive individuals had a CTL response to this epitope • An R to T substitution at position 4 abrogates specific lysis, but not binding to B*3501				
Nef (68–76)	Nef (72–80)	FPVRPQVPL	HIV-1 infection	human (B*3501)	Tomiyama2000a
	• CD8+ T-cells that bound one of six HIV-specific B*3501-epitope tetramers did not express CD28 or CD45A • A significant increase in CD28-CD45RA- cells and a decrease of CD28+CD45RA+ cells was observed in chronically HIV-1-infected individuals relative to healthy individuals • CD28-CD45RA- cells are likely to be effector cells and have high levels of perforin in their cytoplasm • The mean percentage of total CD28- CD8+ cells in chronically infected HIV-1-infected patients was 76.6% in comparison to HIV-1-uninfected individuals (40.6%)				
Nef (68–76)	Nef (72–80 SF2)	FPVRPQVPL	HIV-1 infection	human (B35)	Shiga1996
	• Binds HLA-B*3501				
Nef (68–76)	(SF2)	FPVRPQVPL	HIV-1 infection	human (B35)	Kawana1999
	• HLA B35 is associated with rapid disease progression • The sequences of 9 previously described HIV-1 B35 CTL epitopes were obtained in 10 HLA B35+ and 19 HLA B35- individuals • 3/9 CTL epitopes had substitutions that were more common in B35+ individuals than in B35- individuals, but this was one of the six that had no B35 associated pattern of mutation				
Nef (68–76)	Nef (66–74)	FPVRPQVPL	HIV-1 infection	human (B35)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
Nef (68–76)	Nef (68–76 BRU)	FPVTPQVPL	HIV-1 infection	human (B35)	Choppin2001
	• Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein. • 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing. • FPVTPQVPL was recognized in 1/13 (8%) of individuals with HLA B7, and 1/12 (8%) of individuals with HLA B35. It was a high affinity HLA binder.				
Nef (68–76)	Nef (68–76)	FPVTPQVPL	in vitro stimulation	human (B7)	Wilson1999b
	• Dendritic cells are the most potent for priming T cell responses – DCs can stimulate autologous CTL responses from T cells cultured from HIV negative donors • Th1-biasing cytokines IL-12 or IFN alpha enhance CTL responses in vitro whether the epitope is delivered by pulsing from peptide, or expressed from within				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• B7 and A2 Nef epitopes were studied – FPVTPQVPL has a high affinity for B7				
Nef (68–76)	Nef (68–76)	FPVTPQVPL	HIV-1 infection	human (B7)	Day2001
	• The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person • Subjects with chronic HIV-1 infection recognized between 2-8 out of 11 B7-restricted epitopes • An acute seroconvertor homozygous for the B7 allele recognized five B7-restricted epitopes • The other acute seroconvertor failed to recognize any of the 11 B7-restricted epitopes tested • The B7-restricted CTL response was highly variable and there was no clearly dominant epitope				
Nef (68–76)	Nef (68–76 BRU)	FPVTPQVPL	HIV-1 infection	human (B7)	Choppin2001
	• Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein. • 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing. • FPVTPQVPL was recognized in 1/13 (8%) of individuals with HLA B7, and 1/12 of individuals with HLA B35. It was a high affinity HLA binder.				
Nef (68–76)	Nef (68–76)	FPVTPQVPL	HIV-1 infection	human (B7)	Yu2002a
	• CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 0/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. Also, none of 4 individuals had detectable responses to this epitope after STI.				
Nef (68–77)	Nef (68–77 LAI)	FPVTPQVPLR	HIV-1 infection	human (B*0702)	Brander2001
	• C. Brander notes this is a B*0702 epitope				
Nef (68–77)	Nef (68–77 LAI)	FPVTPQVPLR	HIV-1 infection	human (B7)	Haas1996
	• There was a high degree of variation in three CTL epitopes in Nef in four slow and non-progressors, and variant specific CTLs arose over time to eliminate variants, indicating immune selection				
Nef (68–77)	Nef (subtype B)	FPVTPQVPLR	HIV-1 infection	human (B7)	Kaul2001c
	• This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative • FPVTPQVPLR was recognized in 1 of the 6 women (ML1203), and the response was present in the last available sample prior to seroconversion, 7 months • 20/20 sequences of the infecting strain had no substitutions in this epitope, all were FPVTPQVPLR, so there was no evidence for escape • The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire • This epitope was recognized in 1/22 HEPS sex worker controls, ML851				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (68–77)	Nef (66–75)	FPVRPQVPLR	HIV-1 infection	human (B7)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
Nef (68–77)	Nef (68–77 SF2)	FPVTPQVPLR	HIV-1 infection	human (B7)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-B7+ individuals that had a CTL response to this epitope broken down by group: 0/4 group 1, 0/3 group 2, and 1/1 group 3				
Nef (68–77)	Nef (68–77)	FPVTPQVPLR	HIV-1 infection, HIV-1 exposed seronegative	human (B7)	Kaul2001a
	• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure • Subject ML 1203 started with CTL responses to A*6802 DTVLEDINL and to B7 FPVTPQVPLR prior to seroconversion, and upon seroconversion acquired additional responses to A*6802 ETAYFILKL which became dominant, B7 TPGPG(V/I)RYPL, B7 IPRRIRQGL, and B7 SPRTLNAWV				
Nef (68–77)	Nef (68–77)	FPVTPQVPLR	HIV-1 infection	human (B7)	Day2001
	• The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person • Subjects with chronic HIV-1 infection recognized between 2-8 out of 11 B7-restricted epitopes • An acute seroconvertor homozygous for the B7 allele recognized five B7-restricted epitopes • The other acute seroconvertor failed to recognize any of the 11 B7-restricted epitopes tested • The B7-restricted CTL response was highly variable and there was no clearly dominant epitope				
Nef (68–77)	Nef (68–76)	FPVTPQVPLR	HIV-1 infection	human (B7)	Yu2002a
	• CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 0/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. Also, none of 4 individuals had detectable responses to this epitope after STI.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (68–81)	Nef (82–95 HXB2)	FPVTPQVPLRMTY	HIV-1 infection	human	Guimaráes2002
	• Nef sequences were obtained from Brazilians to study epitope diversity in this geographic region—the HXB2 sequence is FPVTPQVPLRMTY, but fpvRpqvplrmty was observed in most Brazilian sequences regardless of the subtype (A, C, D and F).				
Nef (68–84)	Nef	FPVRPQVPLRPMTYKGA		human	Jubier-Maurin1999
	• 41 new HIV-1 strains describing envelope subtypes of HIV-1 A-H were genetically characterized in the nef region – 34 subtypes were classified in the same subtype in nef and env and 7 of the 41 strains were recombinants • This region was defined as a CTL epitope region that is conserved among HIV-1 M group subtypes				
Nef (71–79)	Nef (71–79 LAI)	TPQVPLRPM	HIV-1 infection	human (B*0702)	Brander2001
	• C. Brander notes this is a B*0702 epitope				
Nef (71–79)	Nef (71–79 BRU)	TPQVPLRPM	HIV-1 infection	human (B35)	Choppin2001
	• Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein. • 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing. • TPQVPLRPM was recognized in 1/10 (10%) of individuals with HLA B7, and 1/10 (10%) of individuals with HLA B35. It was a moderate affinity HLA binder.				
Nef (71–79)	Nef (71–79 SF2)	TPQVPLRPM	HIV-1 infection	human (B7)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-B7+ individuals that had a CTL response to this epitope broken down by group: 0/4 group 1, 0/3 group 2, and 1/1 group 3				
Nef (71–79)	Nef (71–79)	TPQVPLRPM	HIV-1 infection	human (B7)	Day2001
	• The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person • Subjects with chronic HIV-1 infection recognized between 2-8 out of 11 B7-restricted epitopes • An acute seroconvertor homozygous for the B7 allele recognized five B7-restricted epitopes • The other acute seroconvertor failed to recognize any of the 11 B7-restricted epitopes tested • The B7-restricted CTL response was highly variable and there was no clearly dominant epitope				
Nef (71–79)	Nef (71–79 BRU)	TPQVPLRPM	HIV-1 infection	human (B7)	Choppin2001
	• Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing. • TPQVPLRPM was recognized in 1/10 (10%) of individuals with HLA B7, and 1/10 (10%) individuals with HLA B35. It was a moderate affinity HLA binder.				
Nef (71–79)	Nef (71–79)	TPQVPLRPM	HIV-1 infection	human (B7)	Yu2002a
	• Epitope name: B7-TM9 • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 0/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. 2/4 individuals had detectable responses to this epitope after STI.				
Nef (71–79)	Nef	TPQVPLRPM	HIV-1 infection	human (B7)	Altfeld2002
	• Epitope name: B7-TM9(Nef) • Peripheral blood (PB) and lymph node (LN) CD8+ T-cell responses were compared in 15 asymptomatic HIV-1 infected patients using all known optimal CTL epitopes (http://hiv-web.lanl.gov/content/hiv-db/REVIEWS/brander2001.html) for each person's class I HLA alleles. • 60 epitope responses were detected in both PB and LN samples of the 15 patients, and an additional 8 responses were detected only in LN. The total magnitude of the response was similar in LN and PB, but the percentage of CD8+ T cells in the LN is lower so the number of HIV-specific cells per million CD8+ T-cells is higher in the LN. • 1 year post-HAART treatment in five patients studied, the magnitude of the CD8 T-cell response was decreased in both LN and PB, but more dramatically in PB, and 13/25 epitope responses in the PB became undetectable, in contrast to 5/26 in the LN. • Treatment interruption following HAART induced resulted in increased viremia accompanied by the restoration of the detection of 13 epitopes that had become undetectable in the PB, and the addition of 9 novel epitope responses. • Breakdowns of epitope responses were shown for 4 individuals. Patient A displayed the greatest response to epitope B14-EL9(gp41), a strong response to B7-TL9(p24), and responses to B7-TM9(Nef) and A32-PW10(RT). Patient C displayed the greatest response to B27-KK10(p24), and in decreasing order also responded to A24-RW8(Nef), B7-IL9(gp41), A24-RL9(gp41), A24-YL8(gp41), and B7-TM9(Nef).				
Nef (71–81)	Nef (75–85 SF2)	RPQVPLRPMTY	HIV-1 infection	human (B*3501)	Tomiyama1997
	• A CTL clone responsive to this epitope was obtained • 4/7 B35-positive individuals had a strong CTL response to this epitope • An R to T substitution at position 1 abrogates specific lysis, but not binding to B*3501 • An R to H substitution at position 7 did not alter reactivity				
Nef (71–81)	Nef (75–85)	RPQVPLRPMTY	HIV-1 infection	human (B*3501)	Tomiyama2000a
	• CD8+ T-cells that bound one of six HIV-specific B*3501-epitope tetramers did not express CD28 or CD45A • A significant increase in CD28-CD45RA- cells and a decrease of CD28+CD45RA+ cells was observed in chronically HIV-1-infected individuals relative to healthy individuals • CD28-CD45RA- cells are likely to be effector cells and have high levels of perforin in their cytoplasm • The mean percentage of total CD28- CD8+ cells in chronically infected HIV-1-infected patients was 76.6% in comparison to HIV-1-uninfected individuals (40.6%)				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (71–81)	Nef (75–85 SF2) • Binds HLA-B*3501	RPQVPLRPMTY	HIV-1 infection	human (B35)	Shiga1996
Nef (71–81)	(SF2) • HLA B35 is associated with rapid disease progression • The sequences of 9 previously described HIV-1 B35 CTL epitopes were obtained in 10 HLA B35+ and 19 HLA B35- individuals • 3/9 CTL epitopes had substitutions that were more common in B35+ individuals than in B35- individuals – only one of these reduced the binding of the peptide to B35 and was shown to be an escape mutation • rpqvplrpmtF was found in 9/10 of the B35+ individuals, none of the B35- individuals—the Y–>F substituted peptide had a similar binding affinity with B35 and was recognized by a CTL clone equally with wildtype.	RPQVPLRPMTY	HIV-1 infection	human (B35)	Kawana1999
Nef (71–81)	Nef (69–79) • One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles	RPQVPLRPMTY	HIV-1 infection	human (B35)	Ferrari2000
Nef (71–81)	Nef (71–81 BRU) • Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein. • 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing. • TPQVPLRPMTY was recognized in 9/12 (75%) of individuals with HLA B7, and 5/10 (50%) of individuals with HLA B35. It was a moderate affinity HLA binder, and the C-term Y readily cleaved in vitro.	TPQVPLRPMTY	HIV-1 infection	human (B35)	Choppin2001
Nef (71–81)	Nef **Vaccine** *Vector/Type:* DNA prime with vaccinia MVA boost *Strain:* subtype A *HIV component:* p17, p24, polyepitope • The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000]. • Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].	RPQVPLRPMTY	HIV-1 infection, Vaccine	human, macaque (B51)	Hanke2000, Wee2002
Nef (71–81)	Nef (71–81 BRU) • Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein. • 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing.	TPQVPLRPMTY	HIV-1 infection	human (B7)	Choppin2001

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• TPQVPLRPMTY was recognized in 9/12 (75%) of individuals with HLA B7, and 5/10 (50%) of individuals with HLA B35. It was a moderate affinity HLA binder, and the C-term Y readily cleaved in vitro.				
Nef (72–86)	Nef (72–86)	PQVPLRPMTYKGAFD	HIV-1 infection	human	Novitsky2002
	• HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
Nef (72–91)	Nef (71–90 SF2)	PQVPLRMTYKAAVDLSHFL	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • Eleven subjects had CTL that could recognize vaccinia-expressed LAI Nef • Three of these 11 had CTL response to this peptide • The responding subjects were HLA-A3, A32, B51, B62; HLA-A11, A24, B8, B53				
Nef (72–91)	Nef (71–90 SF2)	PQVPLRPMTYKAAVDLSHFL	HIV-1 infection	human	Lieberman1997b
	• CTL expanded ex vivo were later infused into HIV-1 infected patients				
Nef (72–91)	Nef (SF2)	PQVPLRRMTYKAAVDLSHFL	HIV-1 infection	human	Altfeld2001a
	• HIV+ individual AC-06 was tested for reactive overlapping peptides spanning all HIV-1 proteins in an ELISPOT and was found to react with 12 peptides from 7 proteins, suggesting that the breadth of CTL responses are underestimated if accessory proteins are not included in the study • Nef peptides PQVPLRRMTYKAAVDLSHFL, KAAVDLSHFLKEKGGLEGLI and EEEEVGFPVTPQVPLRPMTY were recognized and the first two share KAAVDLSHFL (a Cw8 epitope), the first and last share PQVPLRPMTY				
Nef (73–82)	Nef (73–82)	QVPLRPMTYK	HIV-1 infection	human	Garcia1997
	• The anti-Nef CTL line P1 specific for this epitope is able to kill target cells via two mechanisms • First: Ca^{2+}-dependent, perforin-dependent Nef-specific lysis • Second: Ca^{2+}-independent, CD95-dependent apoptosis that could also kill non-specific targets • Findings indicate that the two mechanisms are not mutually exclusive in human CTL, as they are in mice • CTL mediated CD95-dependent apoptosis may play a role in pathogenesis				
Nef (73–82)	Nef (73–82 NL43)	QVPLRPMTYK	HIV-1 infection	human (A*0301)	Koenig1990
	• 81 Tyr is critical for binding to A3.1 • C. Brander notes that this is an A*0301 epitope in the 1999 database				
Nef (73–82)	Nef (73–82 LAI)	QVPLRPMTYK		human (A*0301)	Brander2001
	• C. Brander notes this is an A*0301 epitope				
Nef (73–82)	Nef	QVPLRPMTYK	HIV-1 infection, Vaccine	human, macaque (A*0301, A11)	Hanke2000, Wee2002
	Vaccine *Vector/Type:* DNA prime with vaccinia MVA boost *Strain:* subtype A *HIV component:* p17, p24, polyepitope • The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000].				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].				
Nef (73–82)		QVPLRPMTYK	HIV-1 infection	human (A03)	Sabbaj2002b
	• Epitope name: Nef-QK10 • Among HIV+ individuals who carried HLA A03, 9/20 (45%) recognized this epitope				
Nef (73–82)	Nef (73–82)	QVPLRPMTYK	HIV-1 infection	human (A11)	Le Borgne2000
	• Soluble factors in supernatant from both an HIV-specific cloned CTL line and an EBV (Epstein-Barr-virus) CTL line inhibit viral replication, but do not block viral entry in CD4+ T lymphocytes, by a noncytotoxic mechanism				
Nef (73–82)	Nef (73–82 LAI)	QVPLRPMTYK	HIV-1 infection	human (A11)	Robertson1993
	• Development of a retroviral vector (pNeoNef) to generate autologous CTL targets • [Hunziker1998] suggests that HLA-A2 does not in fact present this epitope • The initial assignment of HLA-A2 presentation for this epitope was based on a serological HLA typing. Subsequently, the authors revisited the issue with genetic HLA typing and found that HLA-A11 was the correct presenting molecule (Dr. Florence Buseyne, Pers. Comm., 2000)				
Nef (73–82)	Nef (73–82 LAI)	QVPLRPMTYK	HIV-1 infection	human (A11)	Couillin1994, Goulder1997a
	• Mutational variation in HIV epitopes in individuals with appropriate HLA types can result in evasion of CTL response • [Goulder1997a] is a review of immune escape that summarizes this study				
Nef (73–82)	Nef (73–82 LAI)	QVPLRPMTYK	HIV-1 infection	human (A11)	Couillin1995
	• Mutations found in this epitope in HLA-A11 positive and negative donors were characterized				
Nef (73–82)	(LAI)	QVPLRPMTYK		(A11)	Brander2001, Buseyne1999
Nef (73–82)	Nef (73–82)	QVPLRPMTYK	HIV-1 infection	human (A11)	Oxenius2000
	• Epitope name: QVP • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable • One of the 2/8 HLA-A11 study subjects recognized this CTL epitope • Patient SC18(HLA A2/11, B8/44, Cw06/0701, DR3/7, DR52/53, DQ2) recognizes the epitopes ACQGVGGPGHK, QVPLRPMTYK, AVDLSHFLK, and one called QIY but not fully described – he had brief therapy upon seroconversion and has had low viral load during 600 days of follow up				
Nef (73–82)	Nef (73–82)	QVPLRPMTYK	HIV-1 infection, HIV-1 exposed seronegative	human (A11)	Kaul2001a
	• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers				
Nef (73–82)	Nef (73–82)	QVPLRPMTYK	HIV-1 infection	human (A11)	Appay2000
	• Combined tetramer and intracellular cytokine staining was used to study the function of circulating CD8+ T cells specific for HIV and CMV				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• HIV-specific CD8+ T cells expressed lower levels of perforin than CMV-specific CD8+ T cells from the same donor, and this was associated with persistent CD27 expression on HIV-specific cells, suggesting impaired maturation • In most donors, between 50% and 95% of the activated virus-specific CD8+ T cells produced IFN-γ and MIP-1β with a distinct subset that failed to produce TNF-α				
Nef (73–82)	Nef (71–80 93TH253 subtype CRF01) • Epitope name: N73-82 • This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand • HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed • This epitope was weakly reactive in HEPS study subjects 265 who was HLA A2/A11 and 128 who was HLA A11/A33, and after a second in vitro stimulation, in study subject 256 who was HLA A11/33, making it the most reactive epitope tested in HLA-A11 HEPS women, with 3/4 responding • This epitope was strongly reactive in HIV+ study subject 053 who carried HLA-A11	QVPLRPMTYK	HIV-1 infection, HIV-1 exposed seronegative	human (A11)	Sriwanthana2001
Nef (73–82)	Nef (71–80 93TH253 subtype CRF01) • HLA-A11 CRF01 (called subtype E in Bond et al.) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive • 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 finding and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified • This epitope was predicted by the EpiMatrix method to be likely to bind to A11, and it served as an epitope in the FSWs, it was one of the six A11 epitopes that had been previously defined • 4/8 tested FSWs recognized this epitope • An HLA-A11 tetramer was made for this epitope, which was recognized by two subjects – only one subject had an expanded tetramer staining T-cell population after in vitro stimulation • This epitope was highly conserved in other subtypes, and exact matches were common	QVPLRPMTYK	HIV-1 infection	human (A11)	Bond2001
Nef (73–82)	Nef • Epitope name: QVP • Using previously defined epitopes [Oxenius2000, Oxenius2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI). • STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.	QVPLRPMTYK	HIV-1 infection	human (A11)	Oxenius2002b
Nef (73–82)	Nef • Four HIV patients with prolonged clinically successful anti-viral therapy but with ongoing evidence of replication and Nef mRNA transcription, showed specific T-cell responses by Elispot and Tetramer staining, maintained for 2-4 years after initiation of HAART. • Nef epitope recognition was detected in all 4 subjects, gp120, Pol and Gag-specific in 1 or 2 subjects – two patients recognized this epitope, one using HLA-A3, one using HLA-A11 • The HIV-specific CD8+ T-cells had an intermediate maturation phenotype characterized by low levels of perforin and high levels of CD27 expression.	QVPLRPMTYK	HIV-1 infection	human (A11)	Appay2002

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (73–82)	Nef (73–81)	QVPLRPMTYK	HIV-1 infection	human (A2, A3, A11, B35)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
Nef (73–82)	Nef (73–82 LAI)	QVPLRPMTYK	HIV-1 infection	human (A3)	Chassin1999
	• Mutations in Nef that flank this epitope, Thr71Lys and Ala83Gly, may account for an observed loss of CTL reactivity, with escape due to the introduction of proteasome processing defects				
Nef (73–82)	Nef (73–82)	QVPLRPMTYK	HIV-1 infection	human (A3)	Durali1998
	• Cross-clade CTL response was studied by determining the CTL activity in seven patients from Bangui, (6 A subtype, and 1 AG recombinant infections) and one A subtype infection from a person living in France originally from Togo, to different antigens expressed in vaccinia • Pol reactivity: 8/8 had CTL to A subtype, and 7/8 to B subtype, and HIV-2 Pol was not tested • Gag reactivity: 7/8 reacted with A or B subtype gag, 3/8 with HIV-2 Gag • Nef reactivity: 7/8 reacted with A subtype, and 5/8 with B subtype, none with HIV-2 Nef • Env reactivity: 3/8 reacted with A subtype, 1/8 with B subtype, none with HIV-2 Env • One of the patients was shown to react to this epitope: QVPLRPMTYK				
Nef (73–82)	Nef (73–82 LAI)	QVPLRPMTYK	HIV-1 infection	human (A3)	Goulder1997e, Goulder1997a
	• Identical twin hemophiliac brothers were both infected with the same batch of factor VIII • Both had a response to this epitope • [Goulder1997a] is a review of immune escape that summarizes this study				
Nef (73–82)	Nef (73–82)	QVPLRPMTYK	HIV-1 infection	human (A3)	Lubaki1997
	• Eighty two HIV-1-specific CTL clones from 5 long-term non-progressors were isolated and analyzed for breadth of response • A sustained Gag, Env and Nef response was observed, and clones were restricted by multiple HLA epitopes, indicating a polyclonal response • An A3+ subject had a strong response to this epitope, with 10/11 CTL clones being specific for this epitope, isolated at two time points, 1 year apart				
Nef (73–82)	Nef (73–82)	QVPLRPMTYK	HIV-1 infection	human (A3)	Samri2000
	• Epitope name: N1 • The epitope was recognized by patients 252#0 and 252#4 in a study of the effects of therapy escape mutations on CTL recognition				
Nef (73–82)	Nef (73–82 SF2)	QVPLRRMTYK	HIV-1 infection	human (A3)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-A3+ individuals that had a CTL response to this epitope broken down by group: 3/7 group 1, 1/4 group 2, and 1/2 group 3				
Nef (73–82)	Nef (SF2)	QVPLRPMTYK	HIV-1 infection	human (A3)	Altfeld2000b
	• This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (73–82)	Nef (73–82)	QVPLRPMTYK	HIV-1 infection	human (A3)	Yu2002a
	• Epitope name: A3-QK10 • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 3/14 HLA-A3 positive individuals had detectable A3-restricted responses to this epitope during acute infection, but only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 5/7 individuals had detectable responses to this epitope after STI.			
Nef (73–82)	Nef	QVPLRPMTYK	HIV-1 infection	human (A3)	Appay2002
	• Four HIV patients with prolonged clinically successful anti-viral therapy but with ongoing evidence of replication and Nef mRNA transcription, showed specific T-cell responses by Elispot and Tetramer staining, maintained for 2-4 years after initiation of HAART. • Nef epitope recognition was detected in all 4 subjects, gp120, Pol and Gag-specific in 1 or 2 subjects – two patients recognized this epitope, one using HLA-A3, one using HLA-A11. • The HIV-specific CD8+ T-cells had an intermediate maturation phenotype characterized by low levels of perforin and high levels of CD27 expression.			
Nef (73–82)	Nef (73–82 LAI)	QVPLRPMTYK	HIV-1 infection	human (A3 supertype)	Mollet2000
	• Epitope name: N1 • A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses • In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished • Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change			
Nef (73–82)	Nef (94–103)	QVPLRPMTYK	HIV-1 infection	human (A3 supertype)	Propato2001
	• Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus • This epitope can bind 3/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801)			
Nef (73–82)	Nef (73–82 BRU)	QVPLRPMTYK	HIV-1 infection	human (A3, A11, B35)	Culmann1991
	• Nef CTL clones from HIV+ donors				
Nef (73–82)	Nef (73–82 LAI)	QVPLRPMTYK	HIV-1 infection	human (A3.1)	Koenig1995
	• Alanine substitutions L76A, R77A, M79A, T80A significantly decreased immunogenicity of peptide • Nef CTL clones (4N225) were infused into an HIV-1 infected volunteer to evaluate effects of infusion on viral load/patient health • Infusion led to outburst of escape variants which resulted in higher viral load/accelerated disease progression				
Nef (73–82)	Nef (73–82)	QVPLRPMTYK	HIV-1 infection	human (A3.1)	Betts2000
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• 1/11 of the A2+ individuals was A3, and responded to QVPLRPMTYK as well as two other A3.1 epitopes				
Nef (73–82)	Nef (73–82)	QVPLRPMTYK	HIV-1 infection	human (B*0301)	Wilson2000a
	• Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load was also found • All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39 • ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK • The subject with A*0201 had a moderatly strong response to SLYNTVATL • Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705 • No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL			
Nef (73–82)	Nef (73–82 LAI)	QVPLRPMTYK		human (B27)	Culmann1998
	• Optimal epitope mapped by peptide titration				
Nef (73–82)	Nef (73–82 LAI)	SVPLRPMTYK	HIV-1 infection	human (B35 or C4)	Buseyne1993a
	• Vertical transmission of HIV ranges from 13% to 39% • Primary assays showed cytotoxic activity against at least one HIV protein was detected in 70% of infected children • Epitopes recognized in five children were mapped using synthetic peptides and secondary cultures • Patient EM13, who had a CTL response to three epitopes in Nef, was infected via blood transfusion after birth and went from CDC stage P2A to P2E during the study				
Nef (73–83)	Nef (73–82 BRU)	QVPLRPMTYKA	HIV-1 infection	human (A3)	Choppin2001
	• Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein. • 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing. • QVPLRPMTYKA was recognized in 9/15 (60%) of individuals with HLA A3. It was a high affinity HLA-A3 binder.				
Nef (74–81)	Nef (74–82)	VPLRPMTY		human (A3)	Carreno1992
	• Included in HLA-A3 binding peptide competition study				
Nef (74–81)	Nef (73–82 LAI)	VPLRPMTY	HIV-1 or HIV-2 infection	human (B*3501)	Brander2001
	• C. Brander notes this is a B*3501 epitope				
Nef (74–81)	Nef (75–82)	VPLRPMTY	Peptide-HLA interaction	human (B*3501)	Smith1996
	• Crystal structure of VPLRPMTY-class I B allele HLA-B*3501 complex				
Nef (74–81)	Nef	VPLRPMTY	HIV-1 infection	human (B*3501)	Ostrowski2000
	• The role of CD4+ T-cell help in expansion of virus-specific memory CTL was studied through co-culture *ex vivo* • Optimal expansion of HIV-1-specific memory CTL depended on CD4+ T cell help in 9 of 10 patients – CD40 ligand trimer (CD40LT) could enhance CTL in the absence of CD4+ T cell help to a variable degree in most of patients				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Those CTL that didn't respond to CD40LT could expand with IL2 present, and IL15 produced by dendritic cells also contributes • The T-helper epitope used for CD4+ T cell stimulation was the universal tetanus helper epitope TET830-843 (QYIKANSKFIGITE)				
Nef (74–81)	Nef (subtype B)	VPLRPMTY	HIV-1 exposed seronegative	human (B35)	Kaul2000
	• 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 gamma-IFN responses in the cervix – systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses • Low risk individuals did not have such CD8+ cells • CD8+ T cell epitopes: DTVLEDINL (3 individuals), SLYNVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women				
Nef (74–81)	Nef	VPLRPMTY	HIV-1 infection	human (B35)	Wilson2000a
	• Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load was also found • All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39 • ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK • The subject with A*0201 had a moderatly strong response to SLYNTVATL • Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705 • No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL			
Nef (74–81)	Nef (73–82 LAI)	VPLRPMTY	HIV-1 or HIV-2 infection	human (B35)	Culmann1991, McMichael1994
	• Review of HIV CTL epitopes – defined by B35 motif found within a larger peptide				
Nef (74–81)	Nef (73–82 LAI)	VPLRPMTY	HIV-1 or HIV-2 infection	human (B35)	Rowland-Jones1995b
	• VPLRPMTY also recognized by CTL from HIV-2 seropositives; epitope is conserved				
Nef (74–81)	Nef	VPLRPMTY	HIV-1 exposed seronegative	human (B35)	Rowland-Jones1998a
	• A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating • The A and D subtype consensus are identical to the B clade epitope				
Nef (74–81)	Nef (75–82)	VPLRPMTY	in vitro stimulation	human (B35)	Lalvani1997
	• A peptide-based protocol was optimized for restimulation of CTLp using optimized peptide and IL-7 concentrations – importantly this protocol does not stimulate a primary response, only secondary – peptide-specific CTLp counts could be obtained via staining with peptide-Class I tetramers • This peptide was one of the B35 presented test peptides used in control experiments showing that the assay gave no activity using lymphocytes from 21 healthy B35 seronegative donors				
Nef (74–81)	Nef (subtype B)	VPLRPMTY	HIV-1 exposed seronegative	human (B35)	Rowland-Jones1998b
	• HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This epitope is conserved among A, B, and D clade viruses				
Nef (74–81)	Nef	VPLRPMTY		human (B35)	Rowland-Jones1999
	• CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5 • In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, • HIV-2 version of this epitope is conserved: VPLRPMTY, and CTLs are cross-reactive – one of five B35 CTL epitopes that are cross-reactive, see also [Rowland-Jones1995b]				
Nef (74–81)	Nef (74–81)	VPLRPMTY	HIV-1 infection	human (B35)	Oxenius2000
	• Epitope name: VPL • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable • One of two HLA B35+ among the eight study subjects recognized this epitope • Patient SC15 (HLA A1/68, B8/35, Bw4/6, Cw4/0704) was given acute and sustained therapy and recognized epitopes PPIPVGDIY and VPLRPMTY during 331 days of HAART treatment				
Nef (74–81)	Nef (75–82)	VPLRPMTY	HIV-1 infection, HIV-1 exposed seronegative	human (B35)	Kaul2001a
	• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure • Subject ML 857 shifted from a A*6802 DTVLEDINL and B35 (H/N)PDIVIYQY response prior to seroconversion to a B35 PPIPVGDIY and B35 VPLRPMTY response post-seroconversion				
Nef (74–81)		VPLRPMTY	HIV-1 infection	human (B35)	Sabbaj2002b
	• Epitope name: Nef-VY8 • Among HIV+ individuals who carried HLA B35, 12/22 (55%) recognized this epitope • Among HIV+ individuals who carried HLA B*5301, 0/11 (0%) recognized this epitope				
Nef (74–81)	Nef (74–81 BRU)	VPLRPMTY	HIV-1 infection	human (B35)	Choppin2001
	• Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein. • 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing. • VPLRPMTY was recognized in 5/16 (31%) of individuals with HLA B35, and it was a moderate affinity HLA binder. Cleavage at the C-term Y was frequent in vitro.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (74–81)		VPLRPMTY	HIV-1 infection, Vaccine	human, macaque (B35)	Hanke2000, Wee2002
	Vaccine *Vector/Type:* DNA prime with vaccinia MVA boost *Strain:* subtype A *HIV component:* p17, p24, polyepitope • The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000]. • Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].				
Nef (74–82)	Nef (73–82)	VPLRPMTYK	Peptide-HLA interaction	human (A11)	Zhang1993
	• Exploration of A11 binding motif				
Nef (75–82)	Nef (75–82 LAI)	PLRPMTYK	HIV-1 infection	human (A*1101)	McMichael1994
	• Review of HIV CTL epitopes • C. Brander notes that this is an A*1101 epitope in the 1999 database				
Nef (75–82)	Nef (75–82 LAI)	PLRPMTYK	HIV-1 infection	human (A*1101)	Brander2001
	• C. Brander notes this is an A*1101 epitope				
Nef (77–85)	Nef (77–85 LAI)	RPMTYKAAL	HIV-1 infection	human (B*0702)	Bauer1997
	• Structural constraints on the Nef protein may prevent escape • Noted in Brander 1999, this database, to be B*0702				
Nef (77–85)	Nef (77–85 LAI)	RPMTYKAAL	HIV-1 infection	human (B*0702)	Brander2001
	• C. Brander notes this is a B*0702 epitope				
Nef (77–85)	Nef (75–83 IIIB)	RPMTYKAAL	HIV-1 infection	human (B7)	Oxenius2001b
	• Study of tetramer staining of B7 around RPMTYKAAL gave quantitative results that were very different than functional measurements based on an ELISPOT assay • Autologous clones were checked and 39/40 clones from two time points had the variant sequence RPMTYKGAL – tetramers based on RPMTYKGAL gave a more intense and uniform staining and bound with higher affinity to the RPMTYKGAL Vbeta14 TCR				
Nef (77–85)	Nef (77–85 SF2)	RPMTYKAAL	HIV-1 infection	human (B7)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-B7+ individuals that had a CTL response to this epitope broken down by group: 1/4 group 1, 0/3 group 2, and 1/1 group 3				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (77–85)	Nef (77–85)	RPMTYKAAL	HIV-1 infection	human (B7)	Day2001
	• The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person • Subjects with chronic HIV-1 infection recognized between 2-8 out of 11 B7-restricted epitopes • An acute seroconvertor homozygous for the B7 allele recognized five B7-restricted epitopes • The other acute seroconvertor failed to recognize any of the 11 B7-restricted epitopes tested • The B7-restricted CTL response was highly variable and there was no clearly dominant epitope			
Nef (77–85)	Nef (77–85)	RPMTYKAAV	HIV-1 infection	human (B7)	Day2001
	• The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person • Subjects with chronic HIV-1 infection recognized between 2-8 out of 11 B7-restricted epitopes • An acute seroconvertor homozygous for the B7 allele recognized five B7-restricted epitopes • The other acute seroconvertor failed to recognize any of the 11 B7-restricted epitopes tested • The B7-restricted CTL response was highly variable and there was no clearly dominant epitope			
Nef (77–85)	Nef (77–85 BRU)	RPMTYKAAV	HIV-1 infection	human (B7)	Choppin2001
	• Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein. • 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing. • RPMTYKAAV was recognized in 7/10 (70%) of individuals with HLA B7, and 0/3 (0%) of individuals with HLA B35. It was a moderate affinity HLA binder.			
Nef (77–85)	Nef (77–85)	RPMTYKAAL	HIV-1 infection	human (B7)	Yu2002a
	• Epitope name: B7-RL9 • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 3/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. 2/4 individuals had detectable responses to this epitope after STI.			
Nef (77–85)	Nef (77–85)	RPMTYKAAV	HIV-1 infection	human (B7)	Yu2002a
	• Epitope name: B7-RV9 • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.			

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• 2/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. 3/4 individuals had detectable responses to this epitope after STI.				
Nef (77–91)	Nef (77–91)	RPMTYKGAFDLSFFL	HIV-1 infection	human	Novitsky2002
	• HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
Nef (79–87)	Nef (81–89 HXB3)	MTYKAALDL	Vaccine	murine (HLA-A201 transgenic)	Sandberg2000
	Vaccine *Vector/Type:* DNA, peptide *Strain:* HXB3 *HIV component:* Nef *Adjuvant:* Freund's adjuvant • Ten Nef 9-mer peptides were predicted to have a strong binding affinity with HLA-A*0201 – of these, four did bind strongly by a T2 class I stabilization assay, several others bound weakly • A CTL immune response to only 3/10 peptides was detected by a 51Cr-release assay after immunization of HLA-A201 transgenic mice with either nef DNA under the control of a CMV promotor coated on, gold particles delivered to abdominal skin by gene gun • MTYKAALDL bound weakly to HLA-A2, but the DNA nef vaccine elicited a good CTL response				
Nef (82–91)	Nef (82–91 LAI)	KAAVDLSHFL	HIV-1 infection	human (C*0802)	Nixon1999
	• A patient who made a mono-specific CTL response to this Nef specific epitope was given effective anti-retroviral therapy within 90 days of infection, reducing the antigenic stimulous • Within 7 days of therapy, his CTLp frequency dropped from 60 to 4 per million PBMC, as his viremia dropped • The patient went from having an activated effector population (detected by CTLp and clone specific RNA) to a non-activated quiescent population (detected by the CTL-clone specific DNA)				
Nef (82–91)	Nef (82–91 LAI)	KAAVDLSHFL	HIV-1 infection	human (C*0802(Cw8))	Brander2001
	• C. Brander notes this is a C*0802(Cw8) epitope				
Nef (82–91)	Nef (82–91 SF2)	KAAVDLSHFL	HIV-1 infection	human (Cw8)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-Cw8+ individuals that had a CTL response to this epitope broken down by group: 1/3 group 1, 0/0 group 2, and 0/1 group 3				
Nef (82–91)	Nef (SF2)	KAAVDLSHFL	HIV-1 infection	human (Cw8)	Altfeld2000b
	• This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual				
Nef (82–96)	Nef (82–96)	KGAFDLSFFLKEKGG	HIV-1 infection	human	Novitsky2002
	• HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This peptide was among the 8 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
Nef (82–101)	Nef (81–100 SF2)	KAAVDLSHFLKEKGGLEGLI	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • Eleven subjects had CTL that could recognize vaccinia-expressed LAI Nef • Three of these 11 had CTL response to this peptide • The responding subjects were HLA-A1, A2, B8, B14; HLA-A11, A24, B8, B53				
Nef (82–101)	Nef (SF2)	KAAVDLSHFLKEKGGLEGLI	HIV-1 infection	human	Altfeld2001a
	• HIV+ individual AC-06 was tested for reactive overlapping peptides spanning all HIV-1 proteins in an ELISPOT and was found to react with 12 peptides from 7 proteins, suggesting that the breadth of CTL responses are underestimated if accessory proteins are not included in the study • Nef peptides PQVPLRRMTYKAAVDLSHFL, KAAVDLSHFLKEKGGLEGLI and EEEEVGFPVTPQVPLRPMTY were recognized and the first two share KAAVDLSHFL (a Cw8 epitope), the first and last share PQVPLRPMTY				
Nef (83–91)	Nef (83–91 BRU)	AAVDLSHFL	HIV-1 infection	human (A2)	Choppin2001
	• Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein. • 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing. • AAVDLSHFL was recognized in 3/18 (17%) of individuals with HLA A2. It was a low affinity HLA binder.				
Nef (83–91)	Nef (85–93 HXB3)	AALDLSHFL	Vaccine	murine (HLA-A201 transgenic)	Sandberg2000
	Vaccine *Vector/Type:* DNA, peptide *Strain:* HXB3 *HIV component:* Nef *Adjuvant:* Freund's adjuvant • Ten Nef 9-mer peptides were predicted to have strong binding affinity for HLA-A*0201 – of these, four did bind strongly by a T2 class I stabilization assay, several others bound weakly • A CTL immune response to only 3/10 peptides was detected by a 51Cr-release assay after immunization of HLA-A201 transgenic mice with nef DNA under the control of a CMV promotor, coated on gold particles delivered to abdominal skin by gene gun • AALDLSHFL was predicted to have a strong binding capacity for HLA-A2, and did, but it was the only one of the peptides recognized that was a strong binder, the other two recognized peptides were weak binders • AALDLSHFL was also tested by subcutaneous injection of Nef peptides in Freund's adjuvant and gave a strong response to the peptide				
Nef (83–92)	Nef (81–90 93TH253 subtype CRF01)	GAFDLSFFLK	HIV-1 infection	human (A11)	Sriwanthana2001
	• Epitope name: N83-92 • This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand • HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed • This epitope was strongly reactive in HIV+ study subjects 053 and 184 who carried HLA-A11.				
Nef (83–92)	Nef (81–90 93TH253 subtype CRF01)	GAFDLSFFLK	HIV-1 infection	human (A11)	Bond2001
	• HLA-A11 CRF01 (called subtype E in Bond et al.) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 finding and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified • This epitope was predicted by the EpiMatrix method to be likely to bind to A11, and it served as an epitope in the FSWs, it was one of the six A11 epitopes that had been previously defined • 4/8 tested FSWs recognized this epitope • This epitope was only conserved in CRF01 and subtype C, and exact matches were uncommon				
Nef (83–94)	Nef (83–94 BRU)	AAVDLSHFLKEK	HIV-1 infection	human (A11)	Culmann1991
	• Epitope defined by boundaries of overlapping peptides that stimulate Nef CTL clones				
Nef (84–91)	Nef (84–91 LAI)	AVDLSHFL	HIV-1 infection	human (Bw62)	Culmann-Penciolelli1994
Nef (84–91)	Nef (84–91)	AVDLSHFL	HIV-1 infection	human (Bw62)	Betts2000
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes • 1/11 of the A2+ individuals that didn't respond to SLYNTVATL reacted with seven other epitopes including this epitope				
Nef (84–92)	Nef (84–92 LAI)	AVDLSHFLK	HIV-1 infection	human (A*1101)	Brander2001
	• C. Brander notes this is an A*1101 epitope				
Nef (84–92)	84 (92–)	AVDLSHFLK	HIV-1 infection	human (A*1101)	Fukada2002
	• Counterparts for eight known clade B HLA A*1101 epitopes were generated for clade E (CRF01). Three epitopes, identical among clade A-E, were cross-reactive and recognized by clade E infected individuals. The clade E and B analogs to three more HLA A*1101 epitopes was recognized in a clade specific manner. Two other HLA A*1101 clade B defined epitopes were found not to have stimulated a response in clade E infected individuals. • AVDLSHFLK was found to elicit clade-specific responses in clade B (AVDLSHFLK is most common, aLdlshflk is a common variant also found in clade A) and clade E (aFdlsFflk is most common and is also common in clade C). AVDLSHFLK was strongly recognized by CTL from 2/5 B clade infected Japanese subjects, as was aLdlshflk, and aFdlsFflk by CTL from 5/7 E clade infected Thai subjects. • The binding of aFdlsFflk to HLA A*1101 was 10-50 times lower than the other variants, and bulk CTL generated from individuals did not cross-react with the cross-clade peptides.				
Nef (84–92)	Nef (84–92 LAI)	AVDLSHFLK	HIV-1 infection	human (A11)	McMichael1994
	• Review of HIV CTL epitopes • C. Brander notes that this is an A*1101 epitope in the 1999 database				
Nef (84–92)	Nef (84–92)	AVDLSHFLK	HIV-1 infection	human (A11)	Betts2000
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes • 1/11 of the A2+ individuals that didn't respond to SLYNTVATL reacted with seven other epitopes including this epitope				
Nef (84–92)	Nef (84–92 LAI)	AVDLSHFLK	HIV-1 infection	human (A11)	Couillin1994, Goulder1997a
	• Mutational variation in HIV epitopes in individuals with appropriate HLA types can result in evasion of CTL response • [Goulder1997a] is a review of immune escape that summarizes this study				
Nef (84–92)	Nef (84–92 LAI)	AVDLSHFLK	HIV-1 infection	human (A11)	Couillin1995
	• Mutations found in this epitope in HLA-A11 positive and negative donors were characterized				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (84–92)	Nef (84–92)	AVDLSHFLK	HIV-1 infection	human (A11)	Oxenius2000
	• Epitope name: AVD • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable • Both of the 2/8 HLA-A11 study subjects recognized this CTL epitope • Patient SC19(HLA A11/12, B8/44, Cw06/0701, DR3/7, DR52/53, DQ 2/8) had a CTL response to epitopes FLKEKGGL, GEIYKRWII, ACQGVGGPGHK, AVDLSHFLK, and FNCGGEFFY that declined during therapy initiated at day 197 • Patient SC18(HLA A2/11, B8/44, Cw06/0701, DR3/7, DR52/53, DQ2) recognizes the epitopes ACQGVGGPGHK, QVPLRPMTYK, AVDLSHFLK, and one called QIY but not fully described – he had brief therapy upon seroconversion and has had low viral load during 600 days of follow up			
Nef (84–92)	Nef (82–90)	AVDLSHFLK	HIV-1 infection	human (A11)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
Nef (84–92)	Nef (84–92 SF2)	AVDLSHFLK	HIV-1 infection	human (A11)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-A11+ individuals that had a CTL response to this epitope broken down by group: 0/3 group 1, 0/0 group 2, and 2/2 group 3				
Nef (84–92)	Nef (84–92)	AVDLSHFLK	HIV-1 infection, HIV-1 exposed seronegative	human (A11)	Kaul2001a
	• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers				
Nef (84–92)	Nef	AVDLSHFLK	HIV-1 infection	human (A11)	Oxenius2002b
	• Epitope name: AVD • Using previously defined epitopes [Oxenius2000, Oxenius2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI). • STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.				
Nef (84–92)	Nef	AVDLSHFLK	HIV-1 infection, Vaccine	human, macaque (A11)	Hanke2000, Wee2002
	Vaccine *Vector/Type:* DNA prime with vaccinia MVA boost *Strain:* subtype A *HIV component:* p17, p24, polyepitope • The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000].				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].				
Nef (84–92)	Nef (84–92 BRU)	AVDLSHFLK	HIV-1 infection	human (A3)	Choppin2001
	• Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein. • 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing. • AVDLSHFLK was recognized in 4/12 (33%) of individuals with HLA A3. It was a high affinity HLA-A3 binder.				
Nef (84–92)	Nef (84–94)	AVDLSHFLK	HIV-1 infection	human (A3)	Yu2002a
	• Epitope name: A3-ALK9 • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 0/14 HLA-A3 positive individuals had detectable A3-restricted responses to this epitope during acute infection, but only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 1/7 individuals began to have detectable responses to this epitope after STI.				
Nef (86–94)	Nef	DLSHFLKEK	HIV-1 infection, Vaccine	human, macaque (A*0301)	Hanke2000, Wee2002
	Vaccine *Vector/Type:* DNA prime with vaccinia MVA boost *Strain:* subtype A *HIV component:* p17, p24, polyepitope • The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000]. • Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].				
Nef (86–94)	Nef (86–94)	DLSHFLKEK	HIV-1 infection, HIV-1 exposed seronegative	human (A3)	Kaul2001a
	• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers				
Nef (86–94)	Nef (84–92 LAI)	DLSHFLKEK	HIV-1 infection	human (A3.1)	McMichael1994
	• Review of HIV CTL epitopes				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (86–100)	Nef (86–100 LAI)	DLSHFLKEKGGLEGL	HIV-1 infection	human (A2)	Robertson1993
	• Development of a retroviral vector (pNeoNef) to generate autologous targets				
Nef (86–100)	Nef (86–100 LAI)	DLSHFLKEKGGLEGL	HIV-1 infection	human (B35)	Buseyne1993b
Nef (86–100)	Nef (86–100 LAI)	DLSHFLKEKGGLEGL	HIV-1 infection	human (B35 or C4)	Buseyne1993a
	• Vertical transmission of HIV ranges from 13% to 39%				
	• Primary assays showed cytotoxic activity against at least one HIV protein was detected in 70% of infected children				
	• Epitopes recognized in five children were mapped using synthetic peptides and secondary cultures				
	• Patient EM13, who had a CTL response to three epitopes in Nef, was infected via blood transfusion after birth and went from CDC stage P2A to P2E during the study				
Nef (87–102)	Nef	FSHFLKEKGGLEGLIY		human	Jubier-Maurin1999
	• 41 new HIV-1 strains describing envelope subtypes of HIV-1 A-H were genetically characterized in the nef region – 34 subtypes were classified in the same subtype in nef and env and 7 of the 41 strains were recombinants				
	• This region was defined as a CTL epitope region that is conserved among HIV-1 M group subtypes				
Nef (88–100)	Nef (103–116)	SHFLKEKGGLEGL	HIV-1 infection	human	Guimaráes2002
	• Nef sequences were obtained from Brazilians to study epitope diversity in this geographic region—most B subtype sequences are SHFLKEKGGLEGL, but sFflkekgglegl is found in most subtype C samples.				
Nef (90–97)	Nef (89–97)	FLKEKGGL	HIV-1 infection	human	Betts2000
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant				
	• 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes				
	• 1/11 of the A2+ individuals that responded to SLYNTVATL reacted with seven other epitopes including this epitope previously described as presented by B8				
Nef (90–97)	Nef	FLKEKGGL	HIV-1 infection	human (A3)	Ostrowski2000
	• The role of CD4+ T-cell help in expansion of virus-specific memory CTL was studied through co-culture *ex vivo*				
	• Optimal expansion of HIV-1-specific memory CTL depended on CD4+ T cell help in 9 of 10 patients – CD40 ligand trimer (CD40LT) could enhance CTL in the absence of CD4+ T cell help to a variable degree in most of patients				
	• Those CTL that didn't respond to CD40LT could expand with IL2 present, and IL15 produced by dendritic cells also contributes				
	• The T-helper epitope used for CD4+ T cell stimulation was the universal tetanus helper epitope TET830-843 (QYIKANSKFIGITE)				
Nef (90–97)		FLKEKGGL	HIV-1 infection	human (B*08)	Sabbaj2002b
	• Epitope name: Nef-FL8				
	• Among HIV+ individuals who carried HLA B*08, 1/3 (33%) recognized this epitope.				
Nef (90–97)	Nef (89–97 LAI)	FLKEKGGL	HIV-1 infection	human (B*0801)	Brander2001
	• C. Brander notes this is a B*0801 epitope				
Nef (90–97)	Nef (89–97 LAI)	FLKEKGGL	HIV-1 infection	human (B8)	Price1997
	• CTL escape variants appeared over time in HLA-B8 HIV-1+ individual, providing evidence of immune escape				
	• Most variants appear at position 5, an anchor residue				
	• FLKE(E,N or Q)GGL showed reduced binding efficiency and recognition				
	• Double mutants (FIKENGGL, FLEENGGL, and FLKGNGGL) completely escaped recognition				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• [Goulder1997a] is a review of immune escape that summarizes this study in the context of CTL escape to fixation				
Nef (90–97)	Nef (90–97 IIIB)	FLKEKGGL	HIV-1 infection	human (B8)	Spiegel1999
	• Study examines the effect of highly active antiretroviral therapy (HAART) on HIV-1 plasma viral load, CTLp and CTLe frequencies in 8 infected children • CTLp (precursors) were measured by stimulating in culture and assaying using 51Cr release, against vaccina expressed IIIB Env, Gag, Pol, Nef • B7-FLKEKGGL tetramer complex was used for one of the children that was HLA-B7, and this infant showed a vigorous response (> 4% of CD8+ T cells) at 9 months of age • HIV-1 specific CTL responses initially increased in children with complete viral suppression, but then decreased, suggesting viral replication is needed to maintain CTL responses				
Nef (90–97)	Nef	FLKEKGGL	Vaccine	human (B8)	Hanke1998a, Hanke1998b
	Vaccine *Vector/Type:* vaccinia *HIV component:* polyepitope • This epitope was shown to be processed and presented to appropriate CTL clones upon infection of human target cells with vaccinia virus Ankara (VVA) carrying 20 HIV-1 epitopes recognized by humans				
Nef (90–97)	Nef (88–95)	FLKEKGGL	HIV-1 infection	human (B8)	Goulder1997g
	• Natural variants for this epitope have been observed in several donors • Substitutions Q5, N5, E5 that alter anchor position 5 are not well recognized • Substitution I2 binds well to B8 and is recognized				
Nef (90–97)	Nef (90–97)	FLKEKGGL	HIV-1 infection	human (B8)	Dyer1999
	• CTL specific responses were measured over a 1.3 to 1.5 year period in members of the Sydney Blood Bank Cohort (SBBC) who had been infected with a natural attenuated strain of HIV-1 which was Nef-defective • Some of these patients had prolonged high levels of CTL effector and memory cells despite low viral load				
Nef (90–97)	Nef (SF2)	FLKEKGGL	HIV-1 infection	human (B8)	Goulder2001a
	• Epitope name: FL8 • This peptide elicited a weak CTL response during acute HIV-1 infection in patient PI004 • Three CTL responses, to epitopes TSTLQEQIGW, ISPRTLNAW, and KAFSPEVIPMF, were evident early after infection; CTL responses to SLYNTVATL, QASQEVKNW, EIYKRWII, and FLKEKGGL were detectable at 5 months post-infection and beyond • FL8 was recognized in an additional patient, AC29, in chronic infection				
Nef (90–97)	Nef (92–99)	FLKEKGGL	HIV-1 infection	human (B8)	Oxenius2001a
	• Epitope name: FLK • Characterization of specific CTL phenotype patterns in response to variation of the virus load in response to antiviral therapy in 3 patients with chronic HIV-1 infection • CTL activation in response to increasing viral load sequential, and co-segregated with apoptosis only during later stages of the response, suggesting antigen-specific cell-death is restricted to distinct CTL sub-populations				
Nef (90–97)	Nef (92–99)	FLKEKGGL	HIV-1 infection	human (B8)	Oxenius2000
	• Epitope name: FLK • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Six of the 7/8 study subjects that were HLA B8 recognized this early dominant CTL epitope • Patient SC2 (HLA A1, B7/8, Cw0701/0702, DR4/53, DQ7) had CTL responsiveness against epitopes FLKEKGGL, GPKVKQWPL, and GEIYKRWII peptides – FLKEKGGL tetramer staining steadily declined and at day 1340 the FLKEKGGL stained cells were no longer detected and the escape mutant FLKENGGI was found in 8/10 clones • Patient SC9 (HLA A1/2, B8/13, Cw0/0701, DR2/11, DQ6/7) had a CTL response against epitopes FLKEKGGL, ILKEPVHGV, SQRRQDILDLWIYHTQGYFPDWQNY, and GEIYKRWII peptides and all responses declined during therapy initiated at day 390 but were restored when therapy become intermittent • Patient SC19(HLA A11/12, B8/44, Cw06/0701, DR3/7, DR52/53, DQ 2/8) had a CTL response to epitopes FLKEKGGL, GEIYKRWII, ACQGVGGPGHK, AVDLSHFLK, and FNCGGEFFY that declined during therapy initiated at day 197 • Patient SC10(HLA A1/3, B8/35, DR1/8, DQ 4/5) had sustained therapy started during acute infection and maintained an immunodominant response to FLKEKGGL and a response to GEIYKRWII through day 1088 • Patient SC12(HLA A1, B8/39, Cw0701/0702, DR2/3, DR51/52, DQ2/6) had sustained therapy started during acute infection and maintained an immunodominant response to FLKEKGGL throughout and minor responses to GEIYKRWII, DCKTILKAL, GGKKKYKLK – GEIYKRWII and GGKKKYKLK responses were stimulated by a brief period off therapy • Patient SC11(HLA A1, B8, Cw0201, DR3/11, DR52, DQ2/7) started therapy early, remained on therapy for 40 days, then reinitiated HAART at day 640 had a CTL response to FLKEKGGL, GPKVKQWPL, and GEIYKRWII throughout and received a benefit from the early limited course therapy				
Nef (90–97)	Nef	FLKEKGGL	HIV-1 infection	human (B8)	Kostense2001
	• HLA tetramers to six epitopes were used to study HLA-A2, B8 and B57 CTL in 54 patients – HIV-specific tetramer positive cells were inversely correlated with viral load in patients with high CD4, but in patients with CD4 T-cells below 400 high tetramer frequencies were found despite high viral load • Most patients have high levels of HIV-specific T-cell expansions, but many of these cells aren't functional • In 15 of the patients, the proportion of IFN gamma producing tetramer cells correlated with AIDS-free survival • Stimulation with HLA-B8 p24 and Nef epitopes significantly increased Nef-specific T-cell numbers in 2 patients (748 and 1113) • There were more functional IFN-gamma producing Nef-specific T-cells within the T-cell population than there were active p24 Gag-specific T-cells • No correlation between elevated numbers of Nef-specific CTL cells and plasma viral load was observed				
Nef (90–97)	Nef (88–95)	FLKEKGGL	HIV-1 infection	human (B8)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
Nef (90–97)	Nef (88–95 SF2)	FLKEKGGL	HIV-1 infection	human (B8)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-B8+ individuals that had a CTL response to this epitope broken down by group: 3/3 group 1, 1/3 group 2, and 1/2 group 3				
Nef (90–97)	Nef (89–97)	FLKEKGGL	HIV-1 infection	human (B8)	Appay2000
	• Combined tetramer and intracellular cytokine staining was used to study the function of circulating CD8+ T cells specific for HIV and CMV • HIV-specific CD8+ T cells expressed lower levels of perforin than CMV-specific CD8+ T cells from the same donor, and this was associated with persistent CD27 expression on HIV-specific cells, suggesting impaired maturation				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• In most donors, between 50% and 95% of the activated virus-specific CD8+ T cells produced IFN-γ and MIP-1β with a distinct subset that failed to produce TNF-α				
Nef (90–97)	Nef (90–97)	FLKEKGGL	HIV-1 infection	human (B8)	Day2001
	• B8-restricted CTL accounted for about 1/3 of the total CTL response in one individual • The response to FLKEKGGL was the second highest response in magnitude compared to all the HLA class I A- and B-restricted epitopes tested in this individual				
Nef (90–97)	Nef	FLKEKGGL	HIV-1 infection	human (B8)	Goulder2000b
	• Tetramer assays were compared with three functional assays in 42 people with chronic HIV infection: ELISPOT, intracellular cytokine staining, and precursor frequency (limiting dilution assay [LDA]) • HIV-specific tetramer staining CTLs appeared to be active, and inert CTL were not found to play a significant role in chronic pediatric or adult HIV infection				
Nef (90–97)	Nef (90–97 BRU)	FLKEKGGL	HIV-1 infection	human (B8)	Choppin2001
	• Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein. • 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing. • FLKEKGGL was recognized in 12/14 (86%) of individuals with HLA B8, and it was a high affinity HLA binder.				
Nef (90–97)	Nef	FLKEKGGL	HIV-1 infection	human (B8)	Oxenius2002b
	• Epitope name: FLK • Using previously defined epitopes [Oxenius2000, Oxenius2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI). • STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.				
Nef (90–97)	Nef	FLKEKGGL	HIV-1 infection	human (B8)	Appay2002
	• Four HIV patients with prolonged clinically successful anti-viral therapy but with ongoing evidence of replication and Nef mRNA transcription, showed specific T-cell responses by Elispot and Tetramer staining, maintained for 2-4 years after initiation of HAART. • Nef epitope recognition was detected in all 4 subjects, gp120, Pol and Gag-specific in 1 or 2 subjects – two patients recognized FLKEKGGL. • The HIV-specific CD8+ T-cells had an intermediate maturation phenotype characterized by low levels of perforin and high levels of CD27 expression.				
Nef (90–97)	Nef	FLKEKGGL	HIV-1 infection	human (B8)	Appay2002
	• Four HIV patients with prolonged clinically successful anti-viral therapy but with ongoing evidence of replication and Nef mRNA transcription, showed specific T-cell responses by Elispot and Tetramer staining, maintained for 2-4 years after initiation of HAART. • Nef epitope recognition was detected in all 4 subjects, gp120, Pol and Gag-specific in 1 or 2 subjects – two patients recognized FLKEKGGL. • The HIV-specific CD8+ T-cells had an intermediate maturation phenotype characterized by low levels of perforin and high levels of CD27 expression.				
Nef (90–97)	Nef	FLKEKGGL	HIV-1 infection, Vaccine	human, macaque (B8)	Hanke2000, Wee2002
	Vaccine *Vector/Type:* DNA prime with vaccinia MVA boost *Strain:* subtype A *HIV component:* p17, p24, polyepitope				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000]. • Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].				
Nef (90–100)	Nef (90–100 BRU)	FLKEKGGLEGL	HIV-1 infection	human (A2)	Choppin2001
	• Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein. • 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing. • FLKEKGGLEGL was recognized in 8/12 (67%) of individuals with HLA A2. It was a low affinity HLA A2 binder.				
Nef (92–100)	(LAI)	KEKGGLEGL		human (B*4001)	Brander2001
	• C. Brander notes this is a B*4001,B60 epitope				
Nef (92–100)		KEKGGLEGL	HIV-1 infection	human (B*4002)	Sabbaj2002b
	• Epitope name: Nef-KL9 • This study monitored epitope responses in HIV-1 infected minority women living in the United States • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release • Patient 01RCH59 was Hispanic, not on HAART, and had a viral load of 5100 and CD4 count of 349 – she also recognized TERQANFL, p2p7p1p6(64-70), HLA-B*4002 and AEWDRVHPV, p24(78-86), HLA-B*4002 • Among HIV+ individuals who carried HLA B40, 3/5 (60%) recognized this epitope				
Nef (92–100)	Nef (90–98 SF2)	KEKGGLEGL	HIV-1 infection	human (B60)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-B60+ individuals that had a CTL response to this epitope broken down by group: 2/2 group 1, 1/1 group 2, and 0/0 group 3				
Nef (92–100)	Nef	KEKGGLEGL	HIV-1 infection	human (B60)	Cao2002
	• KM is a B60 restricted CTL clone that recognizes KEKGGLEGL. • CTL could be activated by a fusion protein of an HIV protein and anthrax lethal factor (LFn-HIV) that promotes antigen presenting cell uptake of exogenous protein and allows processing through the MHC class I pathway. This strategy for CTL detection could allow antigen presentation without generation of cells by the standard methods of using live viral vectors carrying a protein, or by loading the cells with peptides and by-passing processing.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (92–100)	Nef (SF2)	KEKGGLEGL	HIV-1 infection	human (B60(B*4001)	Altfeld2000b
	• This epitope was the dominant B60 (encoded by B*4001) response in 6/8 HLA-B60 individuals, and recognized in all eight • This epitope was also recognized two expressing HLA-B61 individuals (B61 is usually encoded by B*4002, but this study did not distinguish between B*4002, B*4003, B*4004, B*4006, and B*4008) • ELISPOT was a rapid an effective method that was used to define five novel B60 epitopes • HLA-B60 is present in 10-20% of the Caucasoid population and B60/B61 are very common in Asian populations				
Nef (92–100)	Nef (92–100)	KEKGGLEGL	HIV-1 infection	human (B60/B61)	Day2001
	• No immunodominant responses were detected to five B61-restricted epitopes tested • All five B60-restricted epitopes were reactive in another subject, and the B60-restricted responses together contributed over one-third of the total CTL response				
Nef (92–112)	Nef (SF2)	KEKGGLEGLIHSQRRQDIL-DL	HIV-1 infection	human	Altfeld2000b
	• This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual • The response to the peptide was CD8 dependent, but the HLA presenting molecule and optimal epitope were not determined				
Nef (92–112)	Nef (SF2)	KEKGGLEGLIHSQRRQDIL-DL	HIV-1 infection	human	Altfeld2000b
	• This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual • The response to the peptide was CD8 dependent, but the HLA presenting molecule and optimal epitope were not determined				
Nef (93–106)	Nef (93–106 BRU)	EKGGLEGLIHSQRR	HIV-1 infection	human (A1, B8)	Hadida1992
	• HIV-1 specific CTLs detected in lymphoid organs of HIV-1 infected patients				
Nef (97–111)	Nef (97–111)	LEGLIYSKKRQEILD	HIV-1 infection	human	Novitsky2002
	• HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
Nef (102–115)	Nef (102–115 LAI)	HSQRRQDILDLWIY	HIV-1 infection	human (B7)	Goulder1997e, Goulder1997a
	• Identical twin hemophiliac brothers were both infected with the same batch of factor VIII • One had a strong response to this peptide, the other did not • [Goulder1997a] is a review of immune escape that summarizes this study				
Nef (102–121)	Nef (101–120 SF2)	HSQRRQDILDLQIYHTQGYF	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • Eleven subjects had CTL that could recognize vaccinia-expressed LAI Nef • Two of these 11 had CTL response to this peptide • The responding subjects were HLA-A2, A3, B8, B62 and HLA-A2, B21				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (103–127)	Nef (103–127 PV22)	SQRRQDILDLWIYHTQGYF-PDWQNY	HIV-1 infection	human (B13)	Jassoy1993
	• HIV-1 specific CTLs release γ-IFN, and α- and β-TNF				
Nef (103–127)	Nef (103–127)	SQRRQDILDLWIYHTQGYF-PDWQNY	HIV-1 infection	human (B13)	Oxenius2000
	• Epitope name: SQR • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable • The only study subject out of eight that was HLA B13+ recognized this epitope • Patient SC9 (HLA A1/2, B8/13, Cw0/0701, DR2/11, DQ6/7) had a CTL response against epitopes FLKEKGGL, ILKEPVHGV, SQRRQDILDLWIYHTQGYFPDWQNY, and GEIYKRWII peptides and all responses declined during therapy initiated at day 390 but were restored when therapy become intermittent				
Nef (105–114)	Nef (105–114 LAI)	RRQDILDLWI	HIV-1 infection	human (B*2705)	Goulder1997c
	• Defined as optimal epitope from within reactive peptide HSQRRQDILDLWIYHTQGYF [Nef(102-121 LAI)] • HLA-B*2705 is associated with slow HIV disease progression • The HLA-B*2705 binding motif includes R at position 2, and L in the C-term position				
Nef (105–114)	Nef (105–114 LAI)	RRQDILDLWI	HIV-1 infection	human (B*2705)	Brander2001
	• C. Brander notes this is a B*2705 epitope				
Nef (105–114)	Nef (105–114 SF2)	RRQDILDLWI	HIV-1 infection	human (B27)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-B27+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 0/0 group 2, and 1/1 group 3				
Nef (105–114)	Nef (105–114)	RRQDILDLWI	HIV-1 infection	human (B27)	Day2001
	• B27-restricted CTL response was strongest to this epitope in one individual				
Nef (105–114)		RRQDILDLWI	HIV-1 infection	human (B27)	Sabbaj2002b
	• Epitope name: Nef-RI10 • Among HIV+ individuals who carried HLA B27, 1/2 (50%) recognized this epitope				
Nef (105–115)	Nef (105–115)	RRQDILDLWIY	HIV-1 infection	human (Cw7)	Yu2002a
	• Epitope name: Cw7-RY11				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• AC-06 was homozygous at all three class I alleles (A3, B7, Cw7), and was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 response to RRQDILDLWIY restricted by HLA-Cw7.				
Nef (106–115)	(LAI)	RQDILDLWIY		(B7)	Brander2001, Goulder1999a
Nef (108–115)		DILDLWIY	HIV-1 infection	human (Cw*0701)	Sabbaj2002b
	• Epitope name: Nef-DY8 • This study monitored epitope responses in HIV-1 infected minority women living in the United States • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release • Subject 03RCH40 was African American, had a viral load of 2500, CD4 count of 372, was not on HAART, and also recognized the epitope ETKLGKAGY, RT(449-457), A*2601 • Among HIV+ individuals who carried HLA Cw07, 2/18 (11%) recognized this epitope				
Nef (112–126)	Nef (112–126)	LWVYHTQGYFPDWQN	HIV-1 infection	human	Novitsky2002
	• HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
Nef (112–133)	Nef (111–132)	LWIYHTQGYFPDWQNYTPG-PGV	HIV-1 infection	human	Lieberman1995
	• HIV-specific CTL lines developed by ex vivo stimulation with peptide				
Nef (112–133)	Nef (111–132 SF2)	LWIYHTQGYFPDWQNYTPG-PGV	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • Eleven subjects had CTL that could recognize vaccinia-expressed LAI Nef • Four of these 11 had CTL response to this peptide • The responding subjects were HLA-A2, B21; HLA-A1, A3, B7, B15; HLA-A2, A26, B7, B38				
Nef (112–133)	Nef (111–132 SF2)	LWIYHTQGYFPDWQNYTPG-PGV	HIV-1 infection	human	Lieberman1997b
	• CTL expanded ex vivo were later infused into HIV-1 infected patients				
Nef (113–125)	Nef (113–125 BRU)	WIYHTQGYFPDWQ	HIV-1 infection	human (B17)	Culmann1989
	• Nef CTL clones from HIV+ donors				
Nef (113–127)	Nef (128–142)	WIYHTQGYFDPWQNY	HIV-1 infection	human	Guimaráes2002
	• Nef sequences were obtained from Brazilians to study epitope diversity in this geographic region – WIYHTQGYFDPWQNY displayed an (H) to (N) substitution in Brazilian Nef-gene subtype C samples, and this substitution is often found in other subtypes tested.				
Nef (113–128)	Nef (113–128 BRU)	WIYHTQGYFPDWQNYT	HIV-1 infection	human (A1)	Hadida1992
	• HIV-1 specific CTLs detected in lymphoid organs of HIV-1 infected patients				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (113–128)	Nef (113–128 LAI)	WIYHTQGYFPDWQNYT	HIV-1 infection	human (A1)	Mollet2000
	• Epitope name: N2 • A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses • In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished • Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change				
Nef (114–127)	Nef	VYHTQGYFPDWQNY	HIV-1 infection	human	Jubier-Maurin1999
Nef (115–125)	Nef (115–125 BRU)	YHTQGYFPDWQ	HIV-1 infection	human (B17)	Culmann1991
	• Nef CTL clones from HIV+ donors				
Nef (116–125)	Nef (116–125 BRU)	HTQGYFPDWQ	HIV-1 infection	human (B*5701)	Brander2001
	• C. Brander notes this is a B*5701 epitope • Subtype of B57 not determined				
Nef (116–125)	Nef (116–125)	HTQGYFPDWQ	HIV-1 infection	human (B57)	Betts2000
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes • One of the A2+ individuals was HLA A*0201, A1, B57 and responded to four B57 epitopes and two others				
Nef (116–125)	Nef (116–125 BRU)	HTQGYFPDWQ	HIV-1 infection	human (B57)	Culmann1991
	• Nef CTL clones from HIV+ donors, optimal peptide mapped				
Nef (116–125)	Nef (116–125)	HTQGYFPDWQ	HIV-1 infection	human (B57)	Oxenius2000
	• Epitope name: HTQ • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable • None of the 8 study subjects recognized this epitope but none were HLA B57+				
Nef (116–125)		HTQGYFPDWQ	HIV-1 infection	human (B57)	Sabbaj2002b
	• Epitope name: Nef-HQ10 • Among HIV+ individuals who carried HLA B57, 0/5 (0%) recognized this epitope				
Nef (117–127)	Nef (117–127)	TQGYFPDWQNY	HIV-1 infection	human	Betts2000
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes • 1/11 of the A2+ individuals was HLA A*0205/A*0208, A30, B27, B44 but responded to HLA Bw62 epitope TQGYFPDWQNY, and one of the other individuals that was A2+, but otherwise of unknown HLA type, reacted with seven epitopes including this one				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (117–127)	Nef (117–127 LAI) • C. Brander notes this is a B*1501 epitope	TQGYFPDWQNY	HIV-1 infection	human (B*1501)	Brander2001
Nef (117–127)	Nef (117–127) • No immunodominant responses were detected to four B62-restricted epitopes tested	TQGYFPDWQNY	HIV-1 infection	human (B62)	Day2001
Nef (117–127)	Nef (117–127 LAI) • Optimal peptide defined by titration	TQGYFPDWQNY	HIV-1 infection	human (Bw62)	Culmann1998
Nef (117–128)	Nef (117–128 BRU) • Nef CTL clones from HIV+ donors	TQGYFPDWQNYT	HIV-1 infection	human (B17, B37)	Culmann1991
Nef (117–147)	Nef (117–147 LAI) **Vaccine** *Vector/Type:* lipopeptide *HIV component:* six peptides • Anti-HIV lipopeptide vaccine consisting of six long amino acid peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial • A CD4+ T cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 1/10 reacted to this Nef peptide • 9/12 tested mounted a CTL response to at least one of the six peptides; each of the six peptides elicited a CTL response in at least one individual • 10/12 tested had an IgG response to this peptide	TQGYFPDWQNYTPGPGVRY-PLTFGWCYKLVP	Vaccine	human	Gahery-Segard2000
Nef (118–127)	Nef (118–127 LAI) • Review of HIV CTL epitopes	QGYFPDWQNY		human (Bw62)	McMichael1994
Nef (120–128)	Nef (120–128) • Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes • 1/11 of the A2+ individuals was HLA A*0205/A*0208, A30, B27, B44 but responded to HLA B37 epitope IYKRWIILGL, and one of the other individuals that was A2+, but otherwise of unknown HLA type, reacted with seven epitopes including this one	YFPDWQNYT	HIV-1 infection	human	Betts2000
Nef (120–128)	Nef (118–126 SF2) • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-A1+ individuals that had a CTL response to this epitope broken down by group: 0/3 group 1, 0/2 group 2, and 1/2 group 3	YFPDWQNYT	HIV-1 infection	human (A1)	Altfeld2001b
Nef (120–128)	Nef (120–128 LAI) • C. Brander notes this is a B*3701 and B*5701 epitope	YFPDWQNYT	HIV-1 infection	human (B*3701)	Brander2001
Nef (120–128)	Nef (120–128 LAI) • C. Brander notes this is a B*5701 epitope • Subtype of B57 not determined	YFPDWQNYT	HIV-1 infection	human (B*5701)	Brander2001

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (120–128)	Nef (120–128 IIIB)	FFPDWKNYT	HIV-1 infection	human (B15)	Wilson1999a
	• This study describes maternal CTL responses in the context of mother-to-infant transmission • Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants • LFPDWKNYT is an escape mutant				
Nef (120–128)	Nef (120–128 LAI)	YFPDWQNYT	HIV-1 infection	human (B37, B57)	Culmann1998
	• Nef CTL clones from HIV+ donors – optimum peptide mapped by titration				
Nef (120–128)		YFPDWQNYT	HIV-1 infection	human (B57)	Sabbaj2002b
	• Epitope name: Nef-YT9 • Among HIV+ individuals who carried HLA B57, 1/5 (20%) recognized this epitope				
Nef (120–144)	Nef (120–144 SF2)	YFPDWQNYTPGPGIRYPLT-FGWCYK	HIV-1 infection	human (A24)	Jassoy1992
	• Epitope recognized by CTL clone derived from CSF				
Nef (122–136)	Nef (122–136)	PDWQNYTPGPGVRYP	HIV-1 infection	human	Novitsky2002
	• HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 8 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
Nef (122–141)	Nef (121–140 SF2)	PDWQNYTPGPGVRYPLTFGW	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • Eleven subjects had CTL that could recognize vaccinia-expressed LAI Nef • Three of these 11 had CTL response to this peptide • The responding subjects were HLA-A2, B21; HLA-A3, A24, B7, B38				
Nef (123–137)	Nef (123–137 IIIB)	QWQNYTPGPGVRYPL	HIV-1 infection	human	Wilson1996
	• Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study • FFPDYTPGPGTRFPL and FFPDYKPGPGTRFPL, naturally occurring variants, were found in mother and are not recognized • LFPDYKPGPGTRFPL and FFPDYKPGPGTRFPL, naturally occurring variants, were found in infant and are not recognized				
Nef (126–135)	Nef (126–135 BRU)	NYTPGPGVRY	HIV-1 infection	human (A24)	Choppin2001
	• Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein. • 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing. • NYTPGPGVRY was recognized in 3/10 (30%) of individuals with HLA A24. It was a moderate affinity HLA-A24 binder.				
Nef (126–138)	Nef (126–138 BRU)	NYTPGPGVRYPLT	HIV-1 infection	human (B7)	Culmann1991
	• Nef CTL clones from HIV+ donors				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (127–141)	Nef (127–141)	YTPGPGVRYPLTFGW	HIV-1 infection	human	Novitsky2002
	• HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 8 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
Nef (128–135)	Nef (128–135 LAI)	TPGPGVRY	in vitro stimulation	human (B*0702)	Lucchiari-Hartz2000
	• Five naturally processed MHC class I ligands were identified in Nef in the conserved immunogenic region Nef between 123-152 • All five could be transported by TAP, and 4/5 had N-termini that were major cleavage points for the proteasome, only one had extended precursor fragments • Both TPGPGVRYPL and TPGPGVRY are naturally processed ligands that can be eluted from HLA-B7 molecules, both are recognized by the same CTL, and both peptides seem to be the direct product of a proteasomal digest • The peptide TPGPGVRY is present in a high copy number, TPGPGVRYPL at a more moderate level, possibly due to a major cleavage site between the Y and P				
Nef (128–136)		TPGPGVRYP	HIV-1 infection	human (B07)	Sabbaj2002b
	• Epitope name: Nef-TP9 • Among HIV+ individuals who carried HLA B07, 4/9 (44%) recognized this epitope				
Nef (128–137)	Nef	TPGPGIRYPL	HIV-1 infection	human	Kaul2001c
	• This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative • The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire • This epitope was recognized by 1/22 HEPS control sex workers, ML851				
Nef (128–137)	Nef (128–137 LAI)	TPGPGVRYPL	HIV-1 infection	human (B*0702)	Brander2001
	• C. Brander notes this is a B*0702 epitope				
Nef (128–137)	Nef (128–137 LAI)	TPGPGVRYPL	in vitro stimulation	human (B*0702)	Lucchiari-Hartz2000
	• Five naturally processed MHC class I ligands were identified in Nef in the conserved immunogenic region Nef between 123-152 • All five could be transported by TAP, and 4/5 had N-termini that were major cleavage points for the proteasome, only one had extended precursor fragments • Both TPGPGVRYPL and TPGPGVRY are naturally processed ligands that can be eluted from HLA-B7 molecules, both are recognized by the same CTL, and both peptides seem to be the direct product of a proteasomal digest • The peptide TPGPGVRY is present in a high copy number, TPGPGVRYPL at a more moderate level, possibly due to a major cleavage site between the Y and P				
Nef (128–137)	Nef (128–137 LAI)	TPGPGVRYPL		human (B*4201)	Brander2001
	• C. Brander notes this is a B*4201 epitope				
Nef (128–137)	Nef (128–137 BRU)	TPGPGVRYPL	HIV-1 infection	human (B35)	Choppin2001
	• Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein. • 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• TPGPGVRYPL was recognized in 8/16 (50%) of individuals with HLA B7, and 1/9 (11%) of individuals with HLA B35. It was a high affinity HLA binder.				
Nef (128–137)		TPGPGVRYPL	HIV-1 infection	human (B7)	Wilson2000a
	• Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load was also found • All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B*2705; and A*0201, A*0301, B*2705, B39 • ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK • The subject with A*0201 had a moderatly strong response to SLYNTVATL • Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705 • No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL			
Nef (128–137)	Nef (128–137 LAI)	TPGPGVRYPL	HIV-1 infection	human (B7)	Haas1996, Haas1997
	• There was a high degree of variation in three CTL epitopes in Nef in four slow and non-progressors, and variant specific CTLs arose over time to eliminate variants, indicating immune selection • The epitope position was taken from [Haas1997]				
Nef (128–137)	Nef	TPGPGVRYPL	HIV-1 exposed seronegative	human (B7)	Rowland-Jones1998a
	• A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating • The D subtype consensus is identical to the B clade epitope • The A subtype consensus is TPGPGIRYPL				
Nef (128–137)	Nef (subtype B)	TPGPGVRYPL	HIV-1 exposed seronegative	human (B7)	Rowland-Jones1998b
	• HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes • This epitope is conserved among B and D clade viruses • The Clade A version of the epitope: TPGPGIRYPL				
Nef (128–137)	Nef (128–137)	TPGPGVRYPL	in vitro stimulation	human (B7)	Wilson1999b
	• Dendritic cells are the most potent for priming T cell responses – DCs can stimulate autologous CTL responses from T cells cultured from HIV negative donors • Th1-biasing cytokines IL-12 or IFN alpha enhance CTL responses in vitro whether the epitope is delivered by pulsing from peptide, or expressed from within • CTL from a B7 donor displayed no reactivity to this epitope, although it had been immunodominant in another study [Haas1996]				
Nef (128–137)	Nef (128–137 SF2)	TPGPGVRYPL	HIV-1 infection	human (B7)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-B7+ individuals that had a CTL response to this epitope broken down by group: 0/4 group 1, 0/3 group 2, and 1/1 group 3				
Nef (128–137)	Nef (128–137)	TPGPGVRYPL	HIV-1 infection, HIV-1 exposed seronegative	human (B7)	Kaul2001a
	• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure • Among HLA-B7 women, 4/5 HEPS and 5/6 HIV-1 infected women recognized this epitope • The dominant response to this HLA allele was to this epitope in 3 of the 4/5 HEPS cases and in 2 of the 5/6 HIV-1 infected women • Subject ML 1203 started with CTL responses to A*6802 DTVLEDINL and to B7 FPVTPQVPLR prior to seroconversion, and upon seroconversion acquired additional responses to A*6802 ETAYFILKL which became dominant, B7 TPGPG(V/I)RYPL, B7 IPRRIRQGL, and B7 SPRTLNAWV				
Nef (128–137)	Nef (128–137)	TPGPGVRYPL	HIV-1 infection	human (B7)	Appay2000
	• Combined tetramer and intracellular cytokine staining was used to study the function of circulating CD8+ T cells specific for HIV and CMV • HIV-specific CD8+ T cells expressed lower levels of perforin than CMV-specific CD8+ T cells from the same donor, and this was associated with persistent CD27 expression on HIV-specific cells, suggesting impaired maturation • In most donors, between 50% and 95% of the activated virus-specific CD8+ T cells produced IFN-γ and MIP-1β with a distinct subset that failed to produce TNF-α				
Nef (128–137)	Nef (128–137)	TPGPGVRYPL	HIV-1 infection	human (B7)	Day2001
	• The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person • Subjects with chronic HIV-1 infection recognized between 2-8 out of 11 B7-restricted epitopes • An acute seroconvertor homozygous for the B7 allele recognized five B7-restricted epitopes • The other acute seroconvertor failed to recognize any of the 11 B7-restricted epitopes tested • The B7-restricted CTL response was highly variable and there was no clearly dominant epitope				
Nef (128–137)	Nef (128–137 BRU)	TPGPGVRYPL	HIV-1 infection	human (B7)	Choppin2001
	• Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein. • 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing. • TPGPGVRYPL was recognized in 8/16 (50%) of individuals with HLA B7, and 1/9 (11%) of individuals with HLA B35. It was a high affinity HLA binder.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (128–137)	Nef	TPGPGVRYPL	HIV-1 infection	human (B7)	Yu2002a
• Epitope name: B7-TL10 • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 0/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. 2/4 individuals had detectable responses to this epitope after STI.					
Nef (128–137)	Nef	TPGPGVRYPL	HIV-1 infection	human (B7)	Appay2002
• Four HIV patients with prolonged clinically successful anti-viral therapy but with ongoing evidence of replication and Nef mRNA transcription, showed specific T-cell responses by Elispot and Tetramer staining, maintained for 2-4 years after initiation of HAART. • Nef epitope recognition was detected in all 4 subjects, gp120, Pol and Gag-specific in 1 or 2 subjects. • The HIV-specific CD8+ T-cells had an intermediate maturation phenotype characterized by low levels of perforin and high levels of CD27 expression.					
Nef (128–137)	Nef	TPGPGVRYPL	HIV-1 infection, Vaccine	human, macaque (B7)	Hanke2000, Wee2002
Vaccine *Vector/Type:* DNA prime with vaccinia MVA boost *Strain:* subtype A *HIV component:* p17, p24, polyepitope • The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000]. • Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].					
Nef (128–137)	Nef (subtype B)	TPGPGVRYPL	HIV-1 exposed seronegative	human (B7(*8101))	Rowland-Jones1998b
• HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes • Clade A version of the epitope: TPGPGIRYPL, clade D version: TPGPGIRYPL					
Nef (128–137)	Nef (128–137 subtype B)	TPGPGVRYPL	HIV-1 exposed seronegative	human (B7, B*8101)	Kaul2000
• 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 gamma-IFN responses in the cervix – systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses • Low risk individuals did not have such CD8+ cells • CD8+ T cell epitopes: DTVLEDINL (3 individuals), SLYNVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women					

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (130–139)	Nef (130–139 BRU)	GPGVRYPLTF	HIV-1 infection	human (B35)	Choppin2001
	• Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein.				
	• 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing.				
	• GPGVRYPLTF was recognized in 0/10 (0%) of individuals with HLA B7, and 1/11 (9%) of individuals with HLA B35, although it was a high affinity HLA binder.				
Nef (130–143)	Nef (130–143 LAI)	GPGVRYPLTFGWCY	HIV-1 infection	human (B*57)	Goulder1996b
	• CTL response to this epitope observed in 4 long-term survivors				
	• Peptide defined on the basis of B*5801 binding motif, yet not cross-restricted except at high concentrations				
Nef (130–143)	Nef (121–141)	GPGVRYPLTFGWCY	HIV-1 infection	human (B57)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari et al. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
Nef (132–144)	Nef	GIRYPLTFGWCFK		human	Jubier-Maurin1999
	• 41 new HIV-1 strains describing envelope subtypes of HIV-1 A-H were genetically characterized in the nef region – 34 subtypes were classified in the same subtype in nef and env and 7 of the 41 strains were recombinants				
	• This region was defined as a CTL epitope region that is conserved among HIV-1 M group subtypes				
Nef (132–147)	Nef (132–147 BRU)	GVRYPLTFGWCYKLVP	HIV-1 infection	human (A1, B8)	Hadida1992
	• HIV-1 specific CTLs detected in lymphoid organs				
Nef (132–147)	Nef (132–147 BRU)	GVRYPLTFGWCYKLVP	HIV-1 infection	human (B18)	Culmann1991
	• Nef CTL clones from HIV+ donors				
Nef (132–147)	Nef (132–147)	GVRYPLTFGWCYKLVP	Vaccine	murine (H-2^d)	Billaut-Mulot2001
	Vaccine *Vector/Type:* DNA with DNA boost, DNA with recombinant protein boost *Strain:* LAI *HIV component:* Gag, Tat, Nef *Adjuvant:* IL18				
	• DNA vaccinated BALB/c mice primed and boosted with the multiepitopic vaccine with IL18 showed lymphoproliferative responses 7 weeks post immunization				
	• Strong but non-lasting HIV-specific CTL responses were detected by a Cr-release assay and DNA prime/DNA boost was more effective than DNA prime protein boost				
	• Immunization with either the multiepitopic DNA or with the mixed DNA vaccine induced HIV-1 specific Th1 cytokines (IL-2 and IFN-gamma)				
	• Co-administration of IL18 increased T-cell responses but decreased anti-HIV antibody levels				
Nef (133–148)	Nef (133–148 LAI)	VRYPLTFGWCYKLVPV		human (B57)	Brander1996b
	• P. Goulder, pers. comm.				
Nef (134–141)	Nef (138–147 LAI)	RYPLTFGW	HIV-1 infection	human (A*2402)	Brander2001
	• C. Brander notes this is an A*2402 epitope				
Nef (134–141)	Nef (138–147 SF2)	RYPLTFGW	HIV-1 infection	human (A24)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-A24+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 2/3 group 2, and 0/0 group 3				
Nef (134–141)	Nef	RYPLTFGW	HIV-1 infection	human (A24)	Altfeld2002
	• Epitope name: A24-RW8(Nef) • Peripheral blood (PB) and lymph node (LN) CD8+ T-cell responses were compared in 15 asymptomatic HIV-1 infected patients using all known optimal CTL epitopes (http://hiv-web.lanl.gov/content/hiv-db/REVIEWS/brander2001.html) for each person's class I HLA alleles. • 60 epitope responses were detected in both PB and LN samples of the 15 patients, and an additional 8 responses were detected only in LN. The total magnitude of the response was similar in LN and PB, but the percentage of CD8+ T cells in the LN is lower so the number of HIV-specific cells per million CD8+ T-cells is higher in the LN. • 1 year post-HAART treatment in five patients studied, the magnitude of the CD8 T-cell response was decreased in both LN and PB, but more dramatically in PB, and 13/25 epitope responses in the PB became undetectable, in contrast to 5/26 in the LN. • Treatment interruption following HAART induced resulted in increased viremia accompanied by the restoration of the detection of 13 epitopes that had become undetectable in the PB, and the addition of 9 novel epitope responses. • Breakdowns of epitope responses were shown for 4 individuals. Patient C displayed the greatest response to B27-KK10(p24), and in decreasing order also responded to A24-RW8(Nef), B7-IL9(gp41), A24-RL9(gp41), A24-YL8(gp41), and B7-TM9(Nef).				
Nef (134–141)	Nef (134–141 LAI)	RYPLTFGW		human (B27)	Culmann1998
	• Optimal peptide defined by titration				
Nef (134–143)	Nef (138–147 SF2)	RYPLTFGWCF	HIV-1 infection	human (A*2402)	Ikeda-Moore1997
	• Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402 • This peptide induced CTL in 3/4 HIV-1+ people tested • RYPLTFGWCF bound to A*2402 strongly, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained				
Nef (134–143)	Nef (138–147)	RYPLTFGWCF	Vaccine	human (A*2402)	Kawana-Tachikawa2002
	Vaccine *Vector/Type:* Sendai virus vector system (SeV) *HIV component:* class I/peptide complexes • Epitope name: Nef138-10 • A Sendai virus vector system (SeV) was developed that expressed HLA-A*2402-restricted class I/peptide complexes; this system could be used to detect responses and has the potential to elicit immune responses. • MHC class I/peptide tetramers could be made using this system that bound to epitope-specific CTLs in PBMCs. • Cells transfection with SeV modified to express A*2402-HIV epitope complexes induced CTL mediated specific cell lysis.				
Nef (134–143)	Nef (134–143 BRU)	RYPLTFGWCY	HIV-1 infection	human (A24)	Choppin2001
	• Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein. • 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing. • RYPLTFGWCY was recognized in 5/12 (42%) of individuals with HLA A24. It was a moderate affinity HLA-A24 binder.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (134–144)	Nef (134–144 LAI)	RYPLTFGWCYK	HIV-1 infection	human (B18)	Couillin1994, Goulder1997a
	• Mutational variation in HIV epitopes in individuals with appropriate HLA types can result in evasion of CTL response • [Goulder1997a] is a review of immune escape that summarizes this study				
Nef (134–144)	Nef (134–144)	RYPLTFGWCYK	HIV-1 infection	human (B18)	Oxenius2000
	• Epitope name: RYP • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable • None of the 8 study subjects recognized this epitope but none were HLA B18+				
Nef (135–143)	Nef (135–143 LAI)	YPLTFGWCY	in vitro stimulation	human (B*0702)	Lucchiari-Hartz2000
	• Five naturally processed MHC class I ligands were identified in Nef in the conserved immunogenic region Nef between 123-152 • All five could be transported by TAP, and 4/5 had N-termini that were major cleavage points for the proteasome, only one had extended precursor fragments • YPLTFGWCY is the naturally processed ligand for B7, and this epitope is the only one of the five that may require trimming at the N-termini • YPLTFGWCY is present in low copy number in the cell, possibly due to a predominant proteasomal cleavage site between Y and P				
Nef (135–143)	Nef (135–143 LAI)	YPLTFGWCY	HIV-1 exposed seronegative	human (B*1801)	Brander2001
	• C. Brander notes this is a B*1801 epitope				
Nef (135–143)		YPLTFGWCY	HIV-1 infection	human (B*5301, B35)	Sabbaj2002b
	• Epitope name: Nef-YY9 • This study monitored epitope responses in HIV-1 infected minority women living in the United States • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release • Subject 00RCH33 was on HAART had a viral load of 2900 and CD4 count of 727 and also recognized the epitopes HIGPGRAFY, gp160(310-318), HLA A*3002; AETFYVDGA, RT(437-445), HLA B*4501; and RSLYNTVATLY, p17(76-86), HLA A*3002 • Among HIV+ individuals who carried HLA B53, 8/15 (53%) recognized this epitope – one subject also carried B7, previously shown to restrict this epitope • Among HIV+ individuals who carried HLA B35, 13/19 (68%) recognized this epitope				
Nef (135–143)	Nef (subtype D)	YPLTFGWCF	HIV-1 exposed seronegative	human (B18)	Kaul2000
	• 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 gamma-IFN responses in the cervix – systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses • Low risk individuals did not have such CD8+ cells • CD8+ T cell epitopes: DTVLEDINL (3 individuals), SLYNVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women				
Nef (135–143)	Nef (135–143 LAI)	YPLTFGWCY	HIV-1 exposed seronegative	human (B18)	Culmann1991, Culmann-Penciolelli1994
	• Nef CTL clones from HIV+ donors				
Nef (135–143)	Nef (135–143 SF2)	YPLTFGWCY	HIV-1 infection	human (B18)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-B18+ individuals that had a CTL response to this epitope broken down by group: 0/3 group 1, 1/2 group 2, and 0/0 group 3				
Nef (135–143)	Nef	YPLTFGWCF	HIV-1 infection	human (B18)	Kaul2002
	• Neisseria gonorrhea cervititis in 9 HIV+ Kenyan sex workers caused a functional deficiency in IFN-gamma production in HIV-1 epitope-specific CD8+ T-cells, detected by intracellular cytokine production and tetramer assays, while not affecting the total number of epitope-specific CTLs. • Ghonorrhea caused the weaker HIV-1 specific CTL responses in 4 HIV-1 exposed persistently seronegative (HEPS) women to become undetectable by Elispot and tetramer assays, and CMV-specific CTL in 2 HEPS subjects were shown to have impaired function with regard to IFN-gamma production.				
Nef (135–143)	Nef	YPLTFGWCY	HIV-1 infection	human (B18)	Altfeld2002
	• Epitope name: B18-YY9(Nef) • Peripheral blood (PB) and lymph node (LN) CD8+ T-cell responses were compared in 15 asymptomatic HIV-1 infected patients using all known optimal CTL epitopes (http://hiv-web.lanl.gov/content/hiv-db/REVIEWS/brander2001.html) for each person's class I HLA alleles. • 60 epitope responses were detected in both PB and LN samples of the 15 patients, and an additional 8 responses were detected only in LN. The total magnitude of the response was similar in LN and PB, but the percentage of CD8+ T cells in the LN is lower so the number of HIV-specific cells per million CD8+ T-cells is higher in the LN. • 1 year post-HAART treatment in five patients studied, the magnitude of the CD8 T-cell response was decreased in both LN and PB, but more dramatically in PB, and 13/25 epitope responses in the PB became undetectable, in contrast to 5/26 in the LN. • Treatment interruption following HAART induced resulted in increased viremia accompanied by the restoration of the detection of 13 epitopes that had become undetectable in the PB, and the addition of 9 novel epitope responses. • Breakdowns of epitope responses were shown for 4 individuals. Patient D displayed the greatest response to B27-KK10 (p24), and also responded to A30-RY11(p17), A32-PW10(RT), A30-KY11(RT), A32-RW10(gp120), and B18-YY9(Nef).				
Nef (135–143)	Nef (135–143)	YPLTFGWCY	HIV-1 infection, HIV-1 exposed seronegative	human (B18, B49)	Kaul2001a
	• Variants YPLTFGWC(Y/F) are specific for the B/D clades • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure • Among HLA-B18 women, 1/4 HEPS and 8/9 HIV-1 infected women recognized this epitope, likelihood ratio 5.3, p value 0.04, and HEPS women tended to respond to FRDYVDRF(Y/F)K, while infected women tended to respond to YPLTFGWC(Y/F) • The dominant response to this HLA allele was to this epitope for the one reactive HEPS case and in all 8/9 HIV-1 infected women • Differences in epitope specificity were only seen for responses restricted by class I HLA alleles A2, A24, A*6802, B14, and B18, previously shown to be associated with resistance to HIV-1 in this cohort				
Nef (135–143)	Nef (139–147 SF2)	YPLTFGWCF	HIV-1 infection	human (B35)	Shiga1996
	• Binds HLA-B*3501				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (135–143)	Nef (135–143 BRU)	YPLTFGWCY	HIV-1 infection	human (B35)	Choppin2001
• Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein. • 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing. • YPLTFGWCY was recognized in 2/13 (15%) of individuals with HLA B7, and 11/14 (79%) of individuals with HLA B35, and it was a moderate affinity HLA binder.					
Nef (135–143)	Nef	YPLTFGWCY	HIV-1 infection	human (B35)	Sabbaj2002a
• IFNgamma T-cell responses in breast milk of 5 HIV-1 infected women from the US and 6 from Zambia were tested with using Elispot. 11/11 women responded to Gag, 8/11 responded to Pol, 7/11 women to Nef, and 2/5 women to Env peptide pools. These responses were shown to be primarily due to CD8+ T-cells in one woman, and another woman had cytolytic responses measured by Cr-release. • T-cells in breast milk from a volunteer who was HLA A3, A11, B35, B51 induced IFNgamma after stimulation with a peptide that carries known B35 epitope YPLTFGWCY. • The frequencies of responses in the two compartments differed, and 2/4 women that responded to epitopes in Nef 101-205 and Pol 601-710 showed responses in breast milk but no detectable responses in peripheral blood cells.					
Nef (135–143)	Nef	YPLTFGWCY	HIV-1 exposed seronegative	human (B49)	Rowland-Jones1998a
• A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating • The A subtype consensus is identical to the B clade epitope • The D subtype consensus is ypltfgwcF.					
Nef (135–143)	Nef (subtype B)	YLPTFGWCY	HIV-1 exposed seronegative	human (B49)	Rowland-Jones1998b
• HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes • This epitope is conserved among A and B clade viruses • The Clade D version of the epitope, YPLTFGWCF, was preferentially recognized by CTL					
Nef (135–143)		YPLTFGWCY	HIV-1 infection	human (B49)	Kaul2001c
• This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative • The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire • This epitope, YPLTFGWC(Y/F), was recognized in 1/22 HEPS sex worker controls (ML1668)					
Nef (135–143)	Nef (135–143 BRU)	YPLTFGWCY	HIV-1 infection	human (B7)	Choppin2001
• Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein.					

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing. • YPLTFGWCY was recognized in 2/13 (15%) of individuals with HLA B7, and 11/14 (79%) of individuals with HLA B35, and it was a moderate affinity HLA binder.				
Nef (136–144)	Nef (136–144 BRU)	PLTFGWCYK	HIV-1 infection	human (A3)	Choppin2001
	• Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein. • 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing. • PLTFGWCYK was recognized in 3/12 (25%) of individuals with HLA A3. It was a low affinity HLA-A3 binder.				
Nef (136–145)	Nef (136–145)	PLTFGWCYKL	in vitro stimulation	human (A*0201)	Wilson1999b
	• Dendritic cells are the most potent for priming T cell responses – DCs can stimulate autologous CTL responses from T cells cultured from HIV negative donors • Th1-biasing cytokines IL-12 or IFN alpha enhance CTL responses in vitro whether the epitope is delivered by pulsing from peptide, or expressed from within • B7 and A2 Nef epitopes were studied and the relative binding affinity of A2 epitopes for A2 was: PLTFGWCYKL greater than VLEWRFDSRL which was much greater than AFHHVAREL • Noted in Brander et al., 1999 this database, to be A*0201				
Nef (136–145)	Nef (136–145 LAI)	PLTFGWCYKL		human (A*0201)	Brander2001
	• C. Brander notes this is an A*0201 epitope				
Nef (136–145)	Nef (136–145 LAI)	PLTFGWCYKL	in vitro stimulation	human (A*0201)	Lucchiari-Hartz2000
	• Five naturally processed MHC class I ligands were identified in Nef in the conserved immunogenic region Nef between 123-152 • All five could be transported by TAP, and 4/5 had N-termini that were major cleavage points for the proteasome, only one had extended precursor fragments • The CTL that recognized PLTFGWCYKL also recognized PLTFGWCYKLV, and both forms of the epitope are naturally processed and both seem to be the direct product of a proteasomal digest, although in low copy number				
Nef (136–145)		PLTFGWCYKL	HIV-1 infection	human (A02)	Sabbaj2002b
	• Epitope name: Nef-PL10 • Among HIV+ individuals who carried HLA A02, 3/29 (10%) recognized this epitope				
Nef (136–145)	Nef (136–145)	PLTFGWCFKL	HIV-1 infection	human (A2)	Durali1998
	• Cross-clade CTL response was studied by determining the CTL activity in seven patients from Bangui, (6 A subtype, and 1 AG recombinant infections) and one A subtype infection from a person living in France originally from Togo, to different antigens expressed in vaccinia • Pol reactivity: 8/8 had CTL to A subtype, and 7/8 to B subtype, and HIV-2 Pol was not tested • Gag reactivity: 7/8 reacted with A or B subtype gag, 3/8 with HIV-2 Gag • Nef reactivity: 7/8 reacted with A subtype, and 5/8 with B subtype, none with HIV-2 Nef • Env reactivity: 3/8 reacted with A subtype, 1/8 with B subtype, none with HIV-2 Env • Patient B18 had the greatest breadth and diversity of response, and recognized Gag SLYNTVATL and Nef PLTFGWCFKL				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (136–145)	Nef (157–166)	PLTFGWCFKL	Vaccine	human (A2)	Woodberry1999

Vaccine *Vector/Type:* DNA prime with vaccinia boost *HIV component:* polyepitope

- A polyepitope vaccine was generated in a vaccinia construct that contiguously encoded seven epitopes, all presented by HLA A-2
- HHD mice have a transgene of HLA A2 linked to the transmembrane and cytotoxic domains of H-2D^d – this transgene is the only MHC molecule expressed in the mice
- CTL responses to Gag (77-85) SLYNTVATL, Pol (476-484) ILKEPVHGV, gp120 (120-128) KLTPLCVTL, and Nef (190-198) AFHHVAREL were observed in HIV polytope HHD-vaccinated mice, and these responses were enhanced with vaccinia boost
- No CTL immune responses were generated against HLA A2-restricted HIV epitopes Nef 157-166 (PLTFGWCYKL), Pol 346-354 (VIYQYMDDL), and Nef 180-189 (VLEWRFDSRL)
- Sixteen HLA A2+ patients were tested for their ability to make CTL responses by peptide restimulation in culture with the epitopes selected for inclusion in the polytope – one individual recognized all seven of these epitopes; 7 patients had CTL cultures able to recognize at least one of the epitopes, and 6 of those 7 recognized more than one epitope, but they were not able to test all peptides for all patients; many patients only had three peptides tested
- PLTFGWCFKL was recognized by 1 of the HLA-A2 patients

Nef (136–145)	Nef (135–144 93TH253 subtype CRF01)	PLTFGWCYKL	HIV-1 infection	human (A2)	Bond2001

- More than half of a cohort of HIV+ female sex workers (FSW) from Northern Thailand were HLA-A11 positive, and this study concentrated on A11 epitopes in this group, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested.
- 0/4 tested FSWs recognized the E clade version of this epitope PLCFGWCFKL, which differs from the previously defined B clade version by two amino acids, PLTFGWCYKL
- This epitope was only conserved in CRF01 (subtype E) and subtype B

Nef (136–145)	Nef (136–145)	PLTFGWCYKL	HIV-1 infection	human (A2)	Day2001

- The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)
- 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person

Nef (136–145)	Nef (136–145 BRU)	PLTFGWCYKL	HIV-1 infection	human (A2)	Choppin2001

- Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein.
- 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing.
- PLTFGWCYKL was recognized in 9/28 (32%) of individuals with HLA A2. It was a low affinity HLA-A2 binder.

Nef (136–146)	Nef (136–146 LAI)	PLTFGWCYKLV	in vitro stimulation	human (A*0201)	Lucchiari-Hartz2000

- Five naturally processed MHC class I ligands were identified in Nef in the conserved immunogenic region Nef between 123-152
- All five could be transported by TAP, and 4/5 had N-termini that were major cleavage points for the proteasome, only one had extended precursor fragments
- The CTL that recognized PLTFGWCYKL also recognized PLTFGWCYKLV, and both forms of the epitope are naturally processed and both seem to be the direct product of a proteasomal digest, although in low copy number

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (137–145)	Nef (158–166)	LTFGWCFKL	HIV-1 infection	human (A2 supertype)	Propato2001
• Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus • This epitope can bind all five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802)					
Nef (137–145)	Nef (139–147 HXB3)	LTFGWCFKL	Vaccine	murine (HLA-A201 transgenic)	Sandberg2000
Vaccine *Vector/Type:* DNA, peptide *Strain:* HXB3 *HIV component:* Nef *Adjuvant:* Freund's adjuvant • Ten Nef 9-mer peptides were predicted to have a strong binding affinity with HLA-A*0201 – of these, four did bind strongly by a T2 class I stabilization assay, several others bound weakly • A CTL immune response to only 3/10 peptides was detected by a 51Cr-release assay after immunization of HLA-A201 transgenic mice with either nef DNA under the control of a CMV promotor, coated on gold particles delivered to abdominal skin by gene gun – LTFGWCFKL did not elicit a CTL response • LTFGWCFKL was also tested by subcutaneous injection of Nef peptides in Freund's adjuvant, because it bound strongly to HLA-A*0201, and the peptide vaccination did elicit a response • The lack of response to the nef DNA vaccine and the response to the peptide suggests LTFGWCFKL may not be processed					
Nef (137–146)	Nef (221A)	LTFGWCFKLV	HIV-1 infection	human (A2)	Altfeld2001c
• Epitope name: Nef-221a • HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested • Three additional previously described HLA-A2 epitopes were added to the set of 20, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acute infected individuals recognized at least 1 (median of 1 and maximum of 2) • 1/22 individuals with chronic HIV-1 infection recognized this epitope in ELISPOT • 2/12 acutely infected individuals recognized this epitope • LTFGWCFKLV binds to five HLA-A2 supertype alleles:A*0203, A*0201 (highest affinity), A*0206, A*6802 and A*0202					
Nef (137–146)	Nef (158–167)	LTFGWCFKLV	HIV-1 infection	human (A2 supertype)	Propato2001
• Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus • This epitope can bind all five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802) • Tetramer staining with A2, beta2microglobulin, and either SLYNTVATL, KLVGKLNWA, or LTFGWCFKL revealed that tetramers detected more HIV-specific sells in LTNP than in progressors, activated effector cells were the minority population, and ELISPOT correlated better with the effector cell subpopulation than the total tetramer stained population					
Nef (162–181)	Nef (161–180)	TSLLHPVSLHGMDDPEREVL	HIV-1 infection	human	Lieberman1995
• HIV-specific CTL lines developed by ex vivo stimulation with peptide					

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (162–181)	Nef (161–180 SF2)	TSLLHPVSLHGMDDPEREVL	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • Eleven subjects had CTL that could recognize vaccinia-expressed LAI Nef • One of these 11 had CTL response to this peptide				
Nef (162–181)	Nef (101–120 SF2)	TSLLHPVSLHGMDDPEREVL	HIV-1 infection	human	Lieberman1997b
	• CTL expanded ex vivo were later infused into HIV-1 infected patients				
Nef (162–181)	Nef (161–180 SF2)	TSLLHPVSLHGMDDPEREVL	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • Eleven subjects had CTL that could recognize vaccinia-expressed LAI Nef • One of these 11 had CTL response to this peptide				
Nef (166–177)	Nef (160–179 SF2)	HPVSLHGMDDPE	HIV-1 infection	human (B35)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-B35+ individuals that had a CTL response to this epitope broken down by group: 1/2 group 1, 0/2 group 2, and 0/1 group 3				
Nef (172–191)	Nef (171–190 SF2)	GMDDPEREVLEWRFDSRLAF	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • Eleven subjects had CTL that could recognize vaccinia-expressed LAI Nef • One of these 11 had CTL response to this peptide • The responding subject was HLA-A2, B21				
Nef (175–184)	Nef (175–184)	DPEKEVLQWK	HIV-1 infection	human (B7)	Jin2000b
	• This a B7 epitope, a subdominant CTL response, was defined by an un-conventional approach used to predict epitopes in an HLA B7+ long-term non-progressor • Three additional sub-dominant HLA B7 epitopes were defined using EpiMatrix, a non-anchor based strategy for defining potential epitopes, which highlighted 2078 possible epitopes in the autologous HIV-1 derived from the study subject, followed by B7 anchor residue prediction which narrowed the set to 55 peptides, three of which could serve as functional CTL epitopes				
Nef (180–189)	Nef (180–189 LAI)	VLEWRFDSRL	HIV-1 infection	human (A*0201)	Haas1996, Haas1997
	• There was a high degree of variation in three CTL epitopes in Nef in four slow and non-progressors, and variant specific CTLs arose over time to eliminate variants, indicating immune selection • Noted in Brander et al., 1999 this database, to be A*0201				
Nef (180–189)	Nef (180–189 LAI)	VLEWRFDSRL		human (A*0201)	Brander2001
	• C. Brander notes this is an A*0201 epitope				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (180–189)	Nef (180–189 LAI)	VLMWQFDSRL	Vaccine	murine (transgenic) (A*0201)	Boissonnas2002
	Vaccine *Vector/Type:* peptide *Strain:* Natural variants *HIV component:* Nef *Adjuvant:* CFA				
	• Ten naturally occurring variants of this epitope were tested for their affinity to HLA-A*0201 and for their ability to induce gamma-IFN and cytotoxic functions through vaccination of HLA-A*0201 transgenic mice.				
	• Only two variants could induce vaccine responses: VLMWQFDSRL, a high affinity binder, and VLQWRFDSRL a medium affinity binder to A*0201.				
	• In vivo priming with Nef peptide VLMWQFDSRL induced cross-reactive CTL to 6/7 peptides tested (AlmwKfdsKl, vlmwKfdsrl, vlmwKfdsKl, vlQwRfdsKl, vlVwrfdTrl, and vlAwKLdsrl but not the LAI peptide vlEwrfdsrl)				
	• In vivo priming with Nef peptide VLQWRFDTRL induced cross-reactive CTL to 3/6 variant Nef peptides (vlMwQfdsrl, vlqwrfdSrl and vlEwrfdsrl).				
Nef (180–189)	Nef (190–198)	VLEWRFDSRL	Vaccine	murine (A*0201)	Singh2002, Sykes1999
	Vaccine *Vector/Type:* DNA *HIV component:* HIV-1 divided into a 32 plasmids in a ubiquitin expression library				
	• C3H (H-2k) transgenic mice carrying a fused HLA-A*0201 alpha1 and alpha2 and H-2Dk alpha3 hybrid class I molecule were immunized using an epidermal gene gun with an ubiquitin expression library of 32 plasmids that spanned the HIV-1 genome. Ubiquitin targets the expressed HIV-1 peptides to the proteasome.				
	• A single immunization with the UB-HIV-1 library vaccine induced potent, stable and multivalent CTL responses against all library members.				
	• Immunodominant epitopes SLYNTVATL (Gag), ILKEPVHGV(Pol), RIQRGPGRAFVTIGK(P18) and AFHHVAREK (Nef) elicited strong CD8+/IFN- responses and stimulated CTL that were functional in a Cr-release assay and against wild type antigen.				
	• The presence of multiple plasmids HLA-A*0201-restricted CTL epitopes did not decrease CTL immunogenicity, and CTL responses to single peptide immunizations were comparable to responses based on mixtures of either 16 or 32 peptides.				
Nef (180–189)	Nef (180–189)	VLEWRFDSRL	in vitro stimulation	human (A2)	Wilson1999b
	• Dendritic cells are the most potent for priming T cell responses – DCs can stimulate autologous CTL responses from T cells cultured from HIV negative donors				
	• Th1-biasing cytokines IL-12 or IFN alpha enhance CTL responses in vitro whether the epitope is delivered by pulsing from peptide, or expressed from within				
	• B7 and A2 Nef epitopes were studied and the relative binding affinity of A2 epitopes for A2 was: PLTFGWCYKL greater than VLEWRFDSRL which was much greater than AFHHVAREL				
Nef (180–189)	Nef (180–189)	VLEWRFDSRL	Vaccine	human (A2)	Woodberry1999
	Vaccine *Vector/Type:* DNA prime with vaccinia boost *HIV component:* polyepitope				
	• A polyepitope vaccine was generated in a vaccinia construct that contiguously encoded seven epitopes, all presented by HLA A-2				
	• HHD mice have a transgene of HLA A2 linked to the transmembrane and cytotoxic domains of H-2D^d – this transgene is the only MHC molecule expressed in the mice				
	• CTL responses to Gag (77-85) SLYNTVATL, Pol (476-484) ILKEPVHGV, gp120 (120-128) KLTPLCVTL, and Nef (190-198) AFHHVAREL were observed in HIV polytope HHD-vaccinated mice, and these responses were enhanced with vaccinia boost				
	• No CTL immune responses were generated against HLA A2-restricted HIV epitopes Nef 157-166 (PLTFGWCYKL), Pol 346-354 (VIYQYMDDL), and Nef 180-189 (VLEWRFDSRL)				
	• Sixteen HLA A2+ patients were tested for their ability to make CTL responses by peptide restimulation in culture with the epitopes selected for inclusion in the polytope – one individual recognized all seven of these epitopes; 7 patients had CTL cultures able to recognize at least one of the epitopes, and 6 of those 7 recognized more than one epitope, but they were not able to test all peptides for all patients; many patients only had three peptides tested				
	• VLEWRFDSRL was recognized by 2 of the HLA-A2 patients				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (180–189)	Nef (180–189 LAI)	VLEWRFDSRL	HIV-1 infection	human (A2)	Mollet2000
	• Epitope name: N3 • A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses • In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished • Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change				
Nef (180–189)	Nef (179–188 93TH253 subtype CRF01)	VLEWRFDSRL	HIV-1 infection	human (A2)	Bond2001
	• More than half of a cohort of HIV+ female sex workers (FSW) from Northern Thailand were HLA-A11 positive, and this study concentrated on A11 epitopes in this group, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested. • 0/4 tested FSWs recognized the E clade version of this epitope VLIWKFDSAL, which differs from the previously defined B clade version by three amino acids, VLEWRFDSRL				
Nef (180–189)	Nef (180–189)	VLEWRFDSRL	HIV-1 infection	human (A2)	Day2001
	• The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person				
Nef (182–198)	Nef (182–198 BRU)	EWRFDSRLAFHHVAREL	HIV-1 infection	human (A1, B8)	Hadida1992
	• HIV-1 specific CTLs detected in lymphoid organs of HIV-1 infected patients				
Nef (182–198)	Nef (182–198 LAI)	EWRFDSRLAFHHVAREL	HIV-1 infection	human (A2, A25(10))	Hadida1995
	• The C-terminal region of Nef (182-205) contains multiple CTL epitopes with 5 distinct HLA restrictions				
Nef (182–198)	Nef (182–198 BRU)	EWRFDSRLAFHHVAREL	HIV-1 infection	human (A25)	Cheynier1992
	• CTL isolated in children born to HIV-1 positive mothers				
Nef (182–198)	Nef (182–198 LAI)	EWRFDSRLAFHHVAREL	HIV-1 infection	human (B35)	Hadida1995
	• The C-terminal region of Nef (182-205) contains multiple CTL epitopes with 5 distinct HLA restrictions				
Nef (182–198)	Nef (182–198 LAI)	EWRFDSRLAFHHVAREL	Vaccine	murine (H-2^d)	VanderRyst1998
	Vaccine *Vector/Type:* Mengo virus, vaccinia *Strain:* LAI *HIV component:* Nef • Macaca mulatta did not have a detectable response to Rec Mengo virus-HIV-1 Nef 65-206 vaccine • BALB/c mice had a weak response to this epitope in the Mengo virus construct – in contrast, HIV-1 Nef induces a strong CTL response in mice when presented in a vaccinia background				
Nef (182–201)	Nef (191–205 SF2)	EWRFDSRLAFHHVARELHPE	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • Eleven subjects had CTL that could recognize vaccinia-expressed LAI Nef • One of these 11 had CTL response to this peptide • The responding subject was HLA-A2, B21				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (182–205)	Nef (182–205 LAI)	EWRFDSRLAFHHVARELHP-EYFKN	Vaccine	human	Gahery-Segard2000
	Vaccine *Vector/Type:* lipopeptide *HIV component:* six peptides • Anti-HIV lipopeptide vaccine consisting of six long amino acid peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial • A CD4+ T cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 4/10 reacted to this Nef peptide • 9/12 tested mounted a CTL response to at least one of the six peptides; each of the six peptides elicited a CTL response in at least one individual • None of the 12 tested had an IgG response to this peptide				
Nef (183–191)		WRFDSRLAF	HIV-1 infection	human (B*1503)	Sabbaj2002b
	• Epitope name: Nef-WF9 • This study monitored epitope responses in HIV-1 infected minority women living in the United States • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release • This epitope was newly defined in this study • Subject 01RCH50 also recognized the epitope RMRGAHTNDV, RT(356-365), A*3002 – she was African American, was on HAART, had a viral load of 960 and CD4 count of 728 • Among HIV+ individuals who carried HLA B15, 3/17 (18%) recognized this epitope				
Nef (186–193)	Nef (186–193 LAI)	DSRLAFHH	HIV-1 infection	human (B35)	Hadida1995
	• The C-terminal region of Nef (182-205) contains multiple CTL epitopes with 5 distinct HLA restrictions				
Nef (186–194)	Nef (186–194)	DSRLAFHHM	HIV-1 infection, HIV-1 exposed seronegative	human (A24)	Kaul2001a
	• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers				
Nef (186–194)	Nef (186–194 BRU)	DSRLAFHHV		human (B51)	Connan1994
	• Resulted in the assembly of HLA-B51				
Nef (188–196)	Nef (188–196 LAI)	RLAFHHVAR	HIV-1 infection	human (B52)	Hadida1995
	• The C-terminal region of Nef (182-205) contains multiple CTL epitopes with 5 distinct HLA restrictions				
Nef (188–201)	Nef (188–201 LAI)	RLAFHHVARELHPE	HIV-1 infection	human (B35 or C4)	Buseyne1993a
	• Vertical transmission of HIV ranges from 13% to 39% • Primary assays showed cytotoxic activity against at least one HIV protein was detected in 70% of infected children • Epitopes recognized in five children were mapped using synthetic peptides and secondary cultures • Patient EM13, who had a CTL response to three epitopes in Nef, was infected via blood transfusion after birth and went from CDC stage P2A to P2E during the study				
Nef (190–198)		ALKHRAYEL	HIV-1 infection	human	Kaul2001c
	• This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative • The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This epitope was in 1/22 HEPS controls, ML1749				
Nef (190–198)	Nef	AFHHVAREL	HIV-1 infection	human (A*0201)	Altfeld2001c
	• Epitope name: Nef AL9 • HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested • Three additional previously described HLA-A2 epitopes were added to the set of 20, including Nef AL9, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acute infected individuals recognized at least 1 (median of 1 and maximum of 2) • RT VL9 was not recognized by any of the 22 HLA-A2 patients with chronic HIV-1 infection or the 13 HLA-A2 patients with acute HIV-1 infection included in this study				
Nef (190–198)	Nef	ALKHRAYEL	HIV-1 infection, Vaccine	human, macaque (A*0201)	Hanke2000, Wee2002
	Vaccine *Vector/Type:* DNA prime with vaccinia MVA boost *Strain:* subtype A *HIV component:* p17, p24, polyepitope • The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000]. • Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].				
Nef (190–198)	Nef (190–198 LAI)	AFHHVAREL	HIV-1 exposed seronegative	human (A2)	Rowland-Jones1998a
	• CTL recognition reported in the context of HLA-B52 and A2.1, A2.2 and A2.4 • A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating • The A subtype consensus is ALKHRAYEL • The D subtype consensus is AfEHKAREm • [Hunziker1998] suggests that HLA-A2 does not in fact present this epitope, and notes that it does not promote A2 assembly [Connan1994] – also see [Brander1998b] • [Hunziker1998] maintains that HLA-A2 does not present this epitope contrary to an earlier report [Hadida1995], (also see [Brander1998a])—despite the position of Hunziker et al., Rowland-Jones and colleagues are confident that this epitope in its A clade form is presented by HLA-A*0201 and A*0202, and it is one of the most common responses seen in both seropositive and exposed-uninfected donors from Nairobi (Rupert Kaul, Pers. Comm.)				
Nef (190–198)	Nef (190–198)	AFHHVAREL	in vitro stimulation	human (A2)	Wilson1999b
	• Dendritic cells are the most potent for priming T cell responses – DCs can stimulate autologous CTL responses from T cells cultured from HIV negative donors • Th1-biasing cytokines IL-12 or IFN alpha enhance CTL responses in vitro whether the epitope is delivered by pulsing from peptide, or expressed from within				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• B7 and A2 Nef epitopes were studied and the relative binding affinity of A2 epitopes for A2 was: PLTFGWCYKL greater than VLEWRFDSRL which was much greater than AFHHVAREL				
Nef (190–198)	Nef (190–198)	AFHHVAREL	Vaccine	human (A2)	Woodberry1999
	Vaccine *Vector/Type:* vaccinia *HIV component:* polyepitope • A polyepitope vaccine was generated in a vaccinia construct that contiguously encoded seven epitopes, all presented by HLA A-2 • HHD mice have a transgene of HLA A2 linked to the transmembrane and cytotoxic domains of H-2D^d – this transgene is the only MHC molecule expressed in the mice • CTL responses to Gag (77-85) SLYNTVATL, Pol (476-484) ILKEPVHGV, gp120 (120-128) KLTPLCVTL, and Nef (190-198) AFHHVAREL were observed in HIV polytope HHD-vaccinated mice, and these responses were enhanced with vaccinia boost • No CTL immune responses were generated against HLA A2-restricted HIV epitopes Nef 157-166 (PLTFGWCYKL), Pol 346-354 (VIYQYMDDL), and Nef 180-189 (VLEWRFDSRL) • Sixteen HLA A2+ patients were tested for their ability to make CTL responses by peptide restimulation in culture with the epitopes selected for inclusion in the polytope – one individual recognized all seven of these epitopes; 7 patients had CTL cultures able to recognize at least one of the epitopes, and 6 of those 7 recognized more than one epitope, but they were not able to test all peptides for all patients; many patients only had three peptides tested • AFHHVAREL was recognized by 2 of the patients				
Nef (190–198)	Nef (190–198 SF2)	AFHHVAREL	HIV-1 infection	human (A2)	Altfeld2001b
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly defined optimal epitopes were tested for CTL response • Number of HLA-A2+ individuals that had a CTL response to this epitope broken down by group: 0/10 group 1, 1/6 group 2, and 0/4 group 3				
Nef (190–198)	Nef (190–198)	ALKHRAYEL	HIV-1 infection, HIV-1 exposed seronegative	human (A2)	Kaul2001a
	• Variants ALKHRAYEL and AFHHVAREL are A/B clade specific • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers				
Nef (190–198)	Nef (subtype B)	AFHHVAREL	HIV-1 exposed seronegative	human (A2, A*0202, A*0201)	Rowland-Jones1998b
	• HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes • Clade A version of the epitope: ALKHRAYEL, Clade D epitope: AFEHKAREM • This epitope was recognized by two different exposed and uninfected prostitutes				
Nef (190–198)	Nef (190–198 LAI)	AFHHVAREK	HIV-1 infection	human (A3)	Hadida1995
	• Naturally occurring L to K anchor substitution abrogates A2 binding, but permits HLA-A3 binding				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (192–206)	Nef (192–206 BRU)	HHVARELHPEYFKNC	HIV-1 infection	human (A1)	Hadida1992
	• HIV-1 specific CTLs detected in lymphoid organs of HIV-1 infected patients				
Nef	Nef (IIIB)		HIV-1 infection	human	Wasik2000
	• HIV+ infants that progressed rapidly to AIDS had lower Th1 responses and decreased production of beta-chemokines and IL-2 relative to other HIV+ infants • No HIV+ infants had no demonstrable CTL at birth, but Th1 responses accompanied by CTL responses developed in children with slowly progressive disease, and not in rapid progressors • CTLp frequencies were determined by limiting dilution using autologous B cells infected with vaccina/HIV constructs				
Nef	Nef		HIV-1 infection	human	De Maria1997
	• CD3+ cells that also carry a natural killer cell receptor (NKR+) can exhibit down regulation of T cell function • Anti-NKR IgM MAb masked this inhibitory function and increased HIV-1 specific CTL activity in phytohemagglutinin-activated PBMC cultured in the presence of IL-2 from 3/5 patients, and in one other case anti-NKR MAb brought HIV-1 specific CTL activity to detectable levels				
Nef	Nef		HIV-1 infection	human	Lubaki1999
	• Three strategies were used to analyze CTL activity: area under the net HIV-specific lysis curve (ACU), linear regression (LR) of net specific lysis, and the standard method, lytic units (LU20) • A correlation between low HIV plasma viral load and increased levels of HIV-specific Gag and Nef CTL activity was observed using ACU and LR, but not LU20				
Nef	Nef (LAI)		Vaccine	human	Gorse1999b
	Vaccine *Vector/Type:* canarypox prime with rgp120 boost *Strain:* LAI and SF2 *HIV component:* Env, Gag, Pro, Nef, Pro • The vaccine used was rec canarypox expressing HIV-1 env, gag, pol, nef and protease (vCP300) with or without administration of HIV-1 SF-2 rgp120 • In vitro inducible CTL activity against HIV-1 Env, Gag, Pol, and Nef antigens was observed in 79% (15 of 19) of vaccine recipients • The combination of vCP300 and vP1291 together resulted in an overall increase in CTL induction and detection sensitivity				
Nef	Nef		HIV-1 infection	human	Gamberg1999
	• 13/13 subjects with advanced HIV infections showed CD8 T cell proliferation and differentiation of CTL in vitro, and six individuals showed HIV-specific responses to Gag, Pol, Env or Nef antigens • Data suggests that the functional and genetic integrity of the CD8 T cell repertoire (TCR betaV gene intrafamily genetic diversity) remains intact through advanced HIV infection, although HIV-specific CTL activity decreases				
Nef	Nef		Vaccine	human	Calarota1999
	Vaccine *Vector/Type:* DNA *HIV component:* Nef, Rev Tat • 9/9 HIV-1+ subjects were given one of three DNA vaccinations for nef, rev or tat, and novel proliferative and CTL responses were generated • The nef DNA immunization induced the highest and most consistent CTLp activity, IFN-gamma production, and IL-6 and IgG responses • Highly active antiretroviral treatment (HAART) did not induce new HIV-specific CTL responses but reduced viral load, while DNA vaccination induced new immune responses but did not reduce viral load – thus this is a potentially complementary and promising combination				
Nef	Nef (LAI)		HIV-1 infection	human	Buseyne1998a
	• This study showed a correlation between strong CTL memory and breadth of response in 7-12 month old infants, and remaining AIDS-free for the first year of life, higher absolute CD4 and CD8 cells, and lower viral load				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef	Nef (LAI)		HIV-1 infection	human	Buseyne1998b
• In infants with positive CTL responses, most responses showed cross-clade reactivity with somewhat diminished recognition of epitopes from different subtypes					
Nef	Nef (LAI)		Vaccine	human	Evans1999
Vaccine *Vector/Type:* canarypox *HIV component:* gp120, gp41, Gag, Pro, Nef, RT					
• A Canarypox vaccine expressing gp120, gp41, Gag, Protease, Nef and Pol CTL epitopes gave rise to CTL that could be detected in 61% of the volunteers – responses to Gag, Env, Nef and Pol were detected 3-6 months after the last vaccination					
Nef	Nef		HIV-1 infection	human	daSilva1998
• CTL dense regions of Nef tend to lie in conserved domains with low non-synonymous substitution per site – authors consider that this may be due to a host adaptation to infection that focuses the CTL response to be directed against conserved functional domains [daSilva1998]					
Nef	Nef (LAI)		HIV-1 infection	human	Legrand1997
• Seventeen recently infected patients were tested for CTL response to HIV proteins Env, Gag, Pol, Rev, Nef, Vif and Tat • An early response (within a month following PI) was noted in 87% of the subjects to Gag, 75% to Env, and 50% to Nef • Early responses to Pol, Rev, Vif and Tat were rare					
Nef	Nef (LAI)		HIV-1 infection	human	Zerhouni1997
• CTL responses to Env, Gag, Nef and RT were tested at various phases of disease progression – 10 asymptomatic patients generally had CTL responses to all proteins, 10 ARC patients responded well to all proteins except Nef, and AIDS patients had few responses to any proteins					
Nef	Nef		HIV-1 infection		Kuiken1999
• A correlation between conserved regions of Nef and CTL epitope density was also noted in [Kuiken1999]. The authors suggest that this may be due to biological reasons such as the one described above [daSilva1998], or due to epitope processing, or may possibly be an artifact of experimental strategy for epitope definition such that conserved epitopes would tend to be identified because they would be more likely to be cross-reactive with the test reagents • Both p17 and Nef show a correlation between epitope density and conserved regions in the protein – in contrast, p24 is a more conserved protein and known epitopes are evenly distributed across p24					
Nef	Nef (BRU)		HIV-1 infection	human	Aladdin1999
• In vitro measurements of CTL-activity by Cr release assay in bulk culture showed no correlation between CTL-activity (gp120, Gag, Pol and Nef) and disease progression as measured by viral load, CD4 and time to death					
Nef	Nef (SF2)		HIV-1 infection	human	Jin1998a
• CTL precursor frequencies were determined in HIV-1 infected pregnant women, and higher CTLp frequencies to Pol and SF2 Nef, but not IIIB Nef, were found in non-transmitting mothers than in transmitting mothers – Nef CTL responses have been found in uninfected infants born to HIV+ women (Lazuriaga95);					
Nef	(subtype C)			human	Novitsky2001
• This study is provides a survey of CTL responses and full length HIV-1 genome sequences from a C subtype infected Botswanan cohort • 37 of 45 subjects (82%) demonstrated Nef specific ELISPOT CTL responses of more than 100 SFC/106 PBMC • Two Nef-immunodominant regions were identified, one spanned amino acid positions 67 to 96 using HXB2 numbering system while the second corresponded to amino acid positions 122 to 141					

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• While there was some subtype B and C cross-reactivity, there was greater breadth and intensity of response if the CTL from HIV-1-infected individuals was probed with ELISPOT using peptides derived from the same subtype (a median of three Nef epitopes recognized within subtype C compared with one Nef epitope recognized from subtype B peptides, and ELISPOT results with a median of 763 SFC/106 PBMC among responses to HIV-1 C, versus a median of 318 SFC/106 PBMC among responses to HIV-1 B				
Nef	Nef (subtype A, B, D)		HIV-1 infection	human	Cao2000
	• HIV-1 subtypes A and D dominate the Ugandan epidemic, and a vaccine trial using B clade antigen is underway – this study addresses relative levels of cross-reactive CTL responses in HIV infected Ugandans to A, D, and B clade recombinant vaccinia viruses expressing Gag, Env, Pol, RT or Nef from HIV-1 clades A, B, and D • Proteins corresponding to the subtype of the infecting strains tended to trigger higher levels of CTL response measured by percent specific lysis, but there was extensive inter-subtype cross-reactivity with B clade proteins and the co-circulating subtype				
Nef	Nef		HIV-1 infection, Vaccine	human	Calarota2001
	Vaccine *Vector/Type:* DNA *HIV component:* Nef, Rev, Tat *Adjuvant:* CpG motifs • This review discusses the cellular immune response, and comments on the stimulatory role of CpG motifs and how HIV-1 DNA vaccines can boost the CTL and Th proliferative responses in asympotomatic HIV+ individuals				
Nef			HIV-1 exposed seronegative	human	De Maria1994, Kuhn2002
	• 6/24 HIV uninfected infants (ages 15-50 months) born to HIV+ mothers had HIV-1 specific CTL responses to vaccinia-expressed Nef, Gag/Pol, Env. • Reviewed in [Kuhn2002].				
Nef			HIV-1 infection	human	Yusim2002
	• Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17. • While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins. • In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed.				
Nef	Nef (HXB)		HIV-1 infection	human	Lu2000a
	• Bacillus anthrax lethal toxin (LFn)-HIV fusion proteins are candidate HIV vaccines that are safe in mice, and LFn-V3 region fusion proteins induce CD8 T cells in BALBc mice. LFn causes exogenous protein to be taken up and processed in a class I pathway. Expressed proteins from Gag p24 and nef fragments cloned into the LFn expression plasmid stimulate gag-specific CD4 proliferation and CTL responses in HIV-infected donor PBMCs in vitro.				
Nef	(BRU)		HIV-1 infection	human	Edwards2002
	• 96% (26/27) chronically infected HIV-1 infected patients elicited gamma-IFN CD8+ T-cell responses against Gag • Nef and/or Pol CTL responses were detected in 86% of the subjects • The magnitude and breadth of Gag and p24 T-cell responses correlated with absolute CD4 counts, and inversely correlated with viral load • Pol and Int CTL responses correlated positively with absolute CD4+ T-cell count • Nef and Env responses did not correlate with either CD4 counts or viral load				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef			HIV-1 infection	human	Larsson2002b
• Autologous mature dendritic cells with rec vaccinia expressing Gag, Pol, Nef and Env could amplify CD8+ T-cell Elispot responses 4-38 fold in five HIV+ patients on successful HAART treatment, relative to autologous monocytes. Some weak responses could only be detected using mature dendritic cells as APCs, and this approach could be useful for detection of low frequency memory cells.					
Nef	(SF2)		HIV-1 and HCV co-infection	human	Lauer2002
• HIV-1 and HCV immune responses were studied in 22 individuals who were co-infected with HIV-1 and hepatitis C virus (HCV). IFNgamma production was measured in an Elispot assay of CD8+ T-cells using targets expressing either Gag, RT, Env and Nef in a vaccinia construct, or one of seven HCV proteins. • All 22 patients targeted at least one protein. 20/22 patients recognized RT, 17/22 patients recognized Gag, 13/22 subjects recognized Env and 11/22 patients recognized Nef. Robust CTL activity was independent of disease progression or viral load. • Despite high HCV viral loads, very few HCV CD8+ T-cell Elispot responses were detected. In a control HCV infected person who did not have HIV-1, strong anti-HCV responses were mounted. • HIV-specific CD4 proliferative responses were detected in 9/17 coinfected patients, but no HCV responses were detected.					
Nef			HIV-1 infection	human	Scott2001
• CTL responses before and after initiation of ART were studied in 13 HIV-1 vertically infected infants <6 months of age, and 4 that were >6 months of age. • Before ART 2/13 infants <6 months of age showed IFNgamma Elispot CD8+ T-cell responses, one to Nef and one to Env and Nef, and these responses became undetectable after successful therapy– 3 infants were coinfected with CMV and all 3 had CMV-specific CD8+ T-cell responses. • One older infant, at 23 months, had CTL responses against all for proteins tested, Gag, Pol, Nef and Env, and had the lowest plasma viremia of the study group. 3/4 infants older than 6 months of age responded to either Nef or Pol. • Administration of ART over 48 weeks broadened the HIV-1-specific CTL response in 2/4 of the older children that were incomplete responders.					
Nef	(IIIB)		HIV-1 infection	human	Ortiz2001
• Immune responses in eight chronically HIV-1 infected patients undergoing HAART therapy structured treatment interruptions (STI) were studied. STI boosted HIV-1 specific CTL responses and elevated CTL responses were maintained up to 22 weeks after the last treatment interruption, but viral load rebound to pretreatment levels and CD4 T-cell count decline was observed. CD8 responses in PBMC were measured by cytokine flow cytometry with gp160, Gag p55, RT-Pol and Nef expressed in vaccinia.					
Nef			Vaccine	murine	Muthumani2002
Vaccine *Vector/Type:* adenovirus *HIV component:* Vpr, Nef, Gag/Pol • Vpr can cause cells to go into G2 arrest, and it surpresses immune cell activation and inflammatory cytokine production, so co-immunization of BALB/c mice with recombinant adenovirus expressing Vpr and HIV-1 antigens Nef or Gag/Pol was tested to see if Vpr reduced the immune response to the other HIV antigens. • Vpr compromised CD8+ T-cell lytic responses and T-helper proliferative responses in mice co-immunized with Vpr and Nef or Gag/Pol. • In vitro, Vpr reduced T-cell cytokine production of IL-12 and TNFalpha, indicative of Vpr-mediated immune suppression.					
Nef	Nef		HIV-1 infection	human (A*0201 and Cw*08)	Shacklett2000
• HIV-1 specific, MHC class I-restricted CTL killing was detected in duodenal and rectal gut associated lymphoid tissue (GALT) sites from three infected individuals – the distribution of class I restricted CTL was different in the peripheral blood samples and GALT samples					
Nef	Nef		HIV-1 infection	human (B*35)	Jin2002
• Patients with HLA-B*35 variants B*3502, B*3503, B*3504, and B*5301 tend to proceed to AIDS more quickly than those with B*3501.					

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Of 32 patients with HLA-B*35 alleles CD8+ CTL responses were quantified using an intracellular cytokine staining assay – 75% had responses to Pol, 69% to Gag, 50% to Nef, and 41% to Env. • The overall magnitude of CTL responses did not differ between those bearing B*3501 and the others. A higher percentage of Gag responses was observed in those that had lower RNA levels that carried B*3501, and there was a negative association with viral load and CTL activity. The data is consistent with higher levels of CTL responses contributing to protection in B*3501 individuals, but not in B*3502, B*3503, B*3504, and B*5301 individuals.				
Nef	Nef (BRU) **Vaccine** *Vector/Type:* DNA *Strain:* BRU *HIV component:* nef		Vaccine	murine (H-2D^d)	Collings1999
	• A comparison of DNA vaccination with HIV-1 Nef expression vectors pBN-CMV-NEF and pBN-RSV-NEF (self-replicating), pCGE2-NEF (non-replicating). • CTL immune responses were detected using all three expression vectors, while a humoral immune response to Nef was only observed in the self-replicating expression vectors; possibly antibody responses require higher levels of protein expression				
Nef	Nef (SIV)		SIV infection	Rhesus macaque (Mamu-A*11, -B*03, -B*04, and -B*17)	Dzuris2000
	• Cell binding assays for Mamu molecules were employed to describe the peptide binding motifs for Mamu-A*11, -B*03, -B*03, -B*04, and -B*17 CTL epitopes – a similarity for Mamu-A*11 and -B*03 and human HLA-B*44 and -B*27, respectively, was observed – all epitopes studied were SIV epitopes, so not specifically listed here				

II-B-21 HIV-1 CTL Epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
HIV-1			HIV-1 infection	human	Schito2001
• Longitudinal analysis (72 weeks) of 15 patients with acute or recent HIV-1 infection implies that HAART treatment alone can not completely conserve CD8+ cell homeostasis and preserve the original T-cell receptor repertoire					
HIV-1			HIV-1 infection	human	Mackewicz2000
• Non-cytotoxic anti-HIV responses of CD8+ T cells cultured with CD4 infected HIV cells are mediated be blocking expression of viral RNA, and do not influence viral replication steps through integration of provirus					
HIV-1			Vaccine		Altes2002
• This study employs a mathematical model to study the consequences of increasing the T-helper response through a vaccine, which would have counter-balancing effects in a new infection: a more intense response provides more help but also more target cells. The model indicates that if the infecting virus had a low replication rate, then CTLp and CD4 helper cells could control an infection. Only a vaccine that could increase CTL responsiveness could reduce viral set point with observed replication rates. • A CD4+ T-cell response without maintained CTL response was deleterious in this model.					
HIV-1			HIV-1 infection	human	Currier2002b
• Elispot standardization was sought using a reference peptide pool of 23, 8-11 mer epitopes from Influenza, cytomegalovirus (CMV), and Epstein Bar Virus (EBV) presented by 11 common HLA class I molecules. • 15/17 (88%) HIV- and 14/20 (70%) HIV+ individuals reacted with this test set and in vitro simulation of the PBMC from these individuals were capable of killing cells expressing the target antigen.					
HIV-1			HIV-1 infection	human, macaque	Wodarz2002
• Mathematical modeling is used to support the idea that T-helper cell dysfunction results in a compromised ability to maintain an anti-HIV CTL memory response. Models suggest strategies to restore CTL memory through therapy and improve long-term immunological control of the virus.					
HIV-1			HIV-1 infection, Vaccine	human	Zinkernagel2002
• HIV immunity and vaccine strategies are compared with to other pathogens. We do not have a successful vaccine agains TB leprosy, HIV, HCV and most parasites, and the author suggests this is associated with the need for a strong T-cell response to these diseases. Vaccine strategies that achieve a physiological low does infection that is well controlled but persists may be required to alter the immunopathological consequences of infection with HIV.					
HIV-1			Vaccine	human	Gaschen2002
• The concept of using an artificial consensus sequence for vaccine design is discussed, comparing the concepts of a model ancestor sequence or a consensus sequence, with illustrations of the potential advantages of the strategy based on C-clade comparisons. • See also a comment [Nickle2003], and reply [Gao2003]					
HIV-1			HIV-1 infection	human, macaque	Johnson2002
• Reviews evidence for CTL escape in HIV epitopes in natural human infections, and in SIV infections of macaque where viral clones with a known time of infection and multiple animals with the same HLA molecules can be tracked. • Vigorous CTL responses are made despite class I down-regulation by the Nef protein, but it may delay cytolysis of infected cells. Too great a loss of MHC proteins may enhance NK cell killing so the fitness advantage of this function of Nef may be in balance.					
HIV-1			HIV-1 infection, Vaccine	human	Newman2002
Vaccine *HIV component:* polyepitope					

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This extensive review covers many aspects of T-cell immunity and natural HIV infections, and considers how this knowledge might be applied to a polyepitope vaccine approach. Strategies concerning ways to avoid the creation of junctional epitopes and use of linkers to enhance processing of such constructs are discussed. • The C-terminal flanking residue (C1) was found to be associated with immunodominance of epitopes, such that R or K (positive charge) > N or Q (amide) > C, G, A, T, S (small) > F, W, Y (aromatic) > I, L, M, V (aliphatic) > D (negative). As this position is outside and proximal to the epitope, processing and cleavage is the likely reason for this observation. • Changing the C1 residue from F to K for an HLA-A2 presented epitope from HBV resulted in a change from the epitope being non-immunogenic to strongly immunogenic.				
HIV-1			HIV-1 infection, Vaccine	human	Johnston2001
	• Reviews the current state of HIV vaccine approaches, and discusses the role of CTL induced immunity in protection or partial protection in animal studies, likening it to the CTL found in HEPS studies.				
HIV-1			HIV-1 infection	human	Klenerman2002
	• The importance of breadth, or spread, of CTL responses is discussed, as narrowly focused responses can be more readily escaped. • Some HLA types and specific epitope recognition may be associated with a better disease outcome. Reasons for this are considered, including NK cell activity, epitope affinity, epitope conservation, and class I specific induction of more effective T-cell receptors.				
HIV-1			HIV-1 infection	human	Kuhn2002
	• Intrauterine exposure of infants to HIV from their mothers results in HIV-1 specific T-helper cell proliferative responses in 1/3 of exposed uninfected babies, and HIV-1 specific CTL in some. Such responses are evident, but it is unknown whether they are associated with lack of infection, but there is some evidence that HIV-1 T-cell responses may reduce transmission in breastfeeding mothers. Summary tables are provided of CD4 and CD8 responses detected in earlier studies.				
HIV-1			HIV-1 infection	human	Kuhn2002, Levy1998
	• A non-HLA-specific, non-chemokine-mediated CD8+ T-cell non-cytotoxic anti-HIV response, measured by suppression of acute viral infection of CD4 cells, was detectable in approximately 16/31 (52%) of uninfected children born of infected mothers, was more commonly detected in those <1 year old, and could reflect a protective response. • Reviewed in [Kuhn2002].				
HIV-1			Vaccine	human	Altes2001
	• Mathematical modeling suggests if the effector CTL vaccine response exceeds the level of response seen in chronic infection, that a memory CTL population is established that can respond very quickly to protect from infection.				
HIV-1			Vaccine	human	Copeland2002
	• This review summarizes cytokines and chemokines produced by CD8+ T-cells that can interfere with HIV's infection and replication.				
HIV-1			Vaccine		Edgeworth2002
	• This review summarizes HIV vaccine strategies, adjuvants, current clinical trials and animal models.				
HIV-1			Vaccine		Graham2002
	• This review summarizes HIV vaccine approaches and clinical trials.				
HIV-1	Env (HXB2)		Vaccine	murine, guinea pig	Chakrabarti2002
	Vaccine *Vector/Type:* DNA *Strain:* HXB2 *HIV component:* gp140deltaCFI, gp160 deletions				

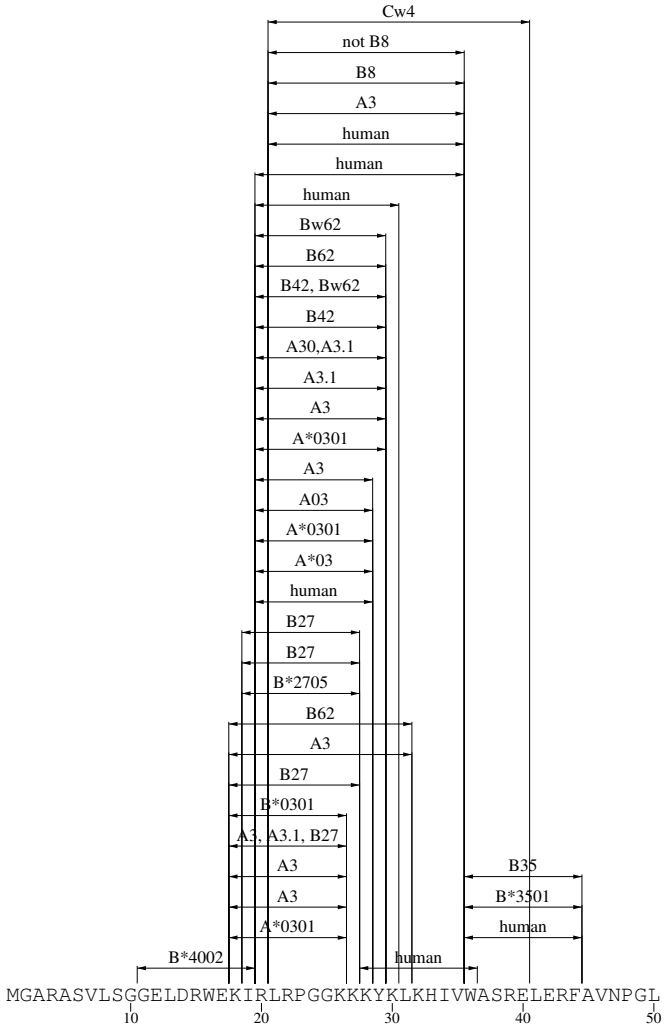
HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Intramuscular injection of plasmid DNA was used to vaccinate BALB/c or Huntley guinea pigs with a series of codon-optimized modified HIV-1 HXB2 envelopes – modifications included elimination of glycosylation sites, deletions, and exchange of the V3 loop to change from a X4 or R5 phenotype. • The mutant envelope gp140deltaCFI gave the most promising result, enhancing antibody responses while retaining the ability to stimulate a strong CTL response. • gp140deltaCFI has deletions in the cleavage site, fusogenic domain and spacing of the heptad repeats, and was designed to mimic a fusion intermediate.				
HIV-1	Env (gp160) (384–467)		Vaccine	rabbit, macaque	Michel1993
	Vaccine *Vector/Type:* hepatitis B surface antigen lipoprotein particles HsBAg *Strain:* LAI *HIV component:* V3 • Immunization with recombinant HIV1 V3/HBsAg hybrid particles into rabbits or macaques elicited and maintained for several months anti-V3 or HIV-1 Env proliferative, CTL and Ab responses.				
HIV-1	Gag (HXB2)		HIV-1 infection	human	Garba2002
	• CD8+ Tcells from 25% of HIV positive individuals produce TGF-beta1 in response to stimulation with HIV proteins, and this can significantly reduce CD8+ T-cell IFN-gamma induction to HIV and vaccinia proteins. • Different peptides can preferentially induce TGF-beta1 or IFN-gamma from CD8+ T-clymphocytes from the same individual, and TGF-beta1 non-specifically suppresses HIV-specific immune responses.				
HIV-1	Pol (HXB2)		HIV-1 infection	human	Garba2002
	• CD8+ Tcells from 25% of HIV positive individuals produce TGF-beta1 in response to stimulation with HIV proteins, and this can significantly reduce CD8+ T-cell IFN-gamma induction to HIV and vaccinia proteins. • Different peptides can preferentially induce TGF-beta1 or IFN-gamma from CD8+ T-clymphocytes from the same individual, and TGF-beta1 non-specifically suppresses HIV-specific immune responses.				
HIV-1	Env (MN)		HIV-1 infection	human	Garba2002
	• CD8+ Tcells from 25% of HIV positive individuals produce TGF-beta1 in response to stimulation with HIV proteins, and this can significantly reduce CD8+ T-cell IFN-gamma induction to HIV and vaccinia proteins. • Different peptides can preferentially induce TGF-beta1 or IFN-gamma from CD8+ T-clymphocytes from the same individual, and TGF-beta1 non-specifically suppresses HIV-specific immune responses.				
HIV-1			Vaccine	human (A11)	Ariyoshi2002
	• This review summarizes issues discussed at a meeting held to discuss options for determining CTL responses to vaccines. Problems are noted: cost for any assay are prohibitive for a Phase III study, Elispot shows interlaboratory variation but could be extended to many samples. HLA-A11 is very common in Thailand – over 30% carry the HLA-A11 allele. Predominant strains may be evolving to evade recognition of A11 restricted epitopes. Few full length CRF01 sequences are available. Epitopes may differ in vaccinees and infected individuals.				
HIV-1			Vaccine	human (B27, B8)	McMichael2002
	• CTL response-eliciting vaccines are reviewed. The natural epitope interactions with the HLA class I presenting molecules and T-cell receptors are described, and the impact of breadth of CTL responses and diversity considered in a vaccine context. • Interesting specific examples are given concerning anchor chain residues. For B27, the B pocket fits Arg (R) but not Lys (K), so even this conservative change is not tolerated. In B8 either R or K can fit in the B pocket, but the substitution will cause conformational shifts in other parts of the epitope.				
HIV-1	gp120 (V3) and p24 (IIIB, MN, BH10)		Vaccine	murine (H-2^d)	Buonaguro2002
	Vaccine *Vector/Type:* virus-like particle *Strain:* gp120 A clade UG5.94UG018, and B clade IIIB *HIV component:* gp120 and Pr55gag				

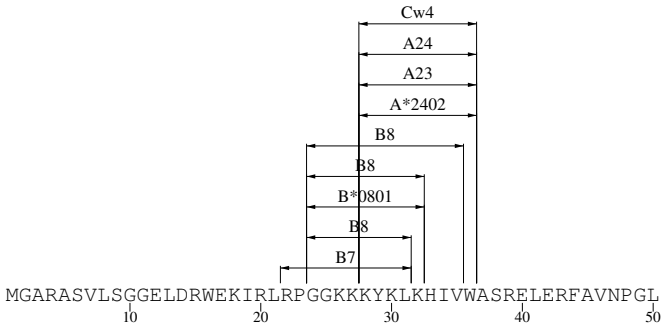
HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• BALB/c mice were given intraperitoneal immunization with virus-like particle (VLPs) expressing recombinant subtype A gp120 and Pr55gag in the absence of adjuvants. • High dose-independent humoral responses against both gp120 and p24 peptides were detected. Antibodies able to elicit 50% neutralization against A clade IIIB and the autologous clade a virus were obtained. • Recombinant rgp120 (clade B, MN) induced T-cell proliferative responses in vitro from vaccinated animals. • CTL activity was observed against splenocytes expressing Env (clade A) and Gag (clade B, BH10) from a vaccinia construct.				
HIV-1			Vaccine	murine (MHC H2d)	Lieberman2002
	Vaccine *Vector/Type:* Listeria monocytogenes *HIV component:* Gag • Attenuated Listeria monocytogenes vectors elicit strong persistent CTL responses in vaccinations of BALB/c mice and can protect mice from a vaccinia-gag challenge.				

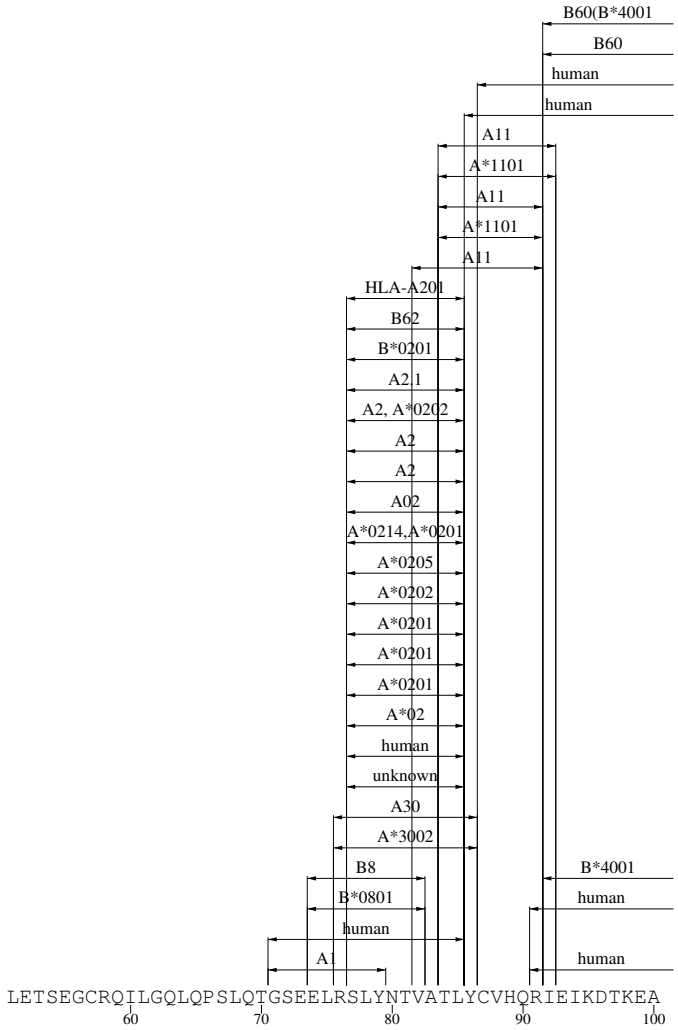
II-C Maps of CTL Epitope Locations Plotted by Protein

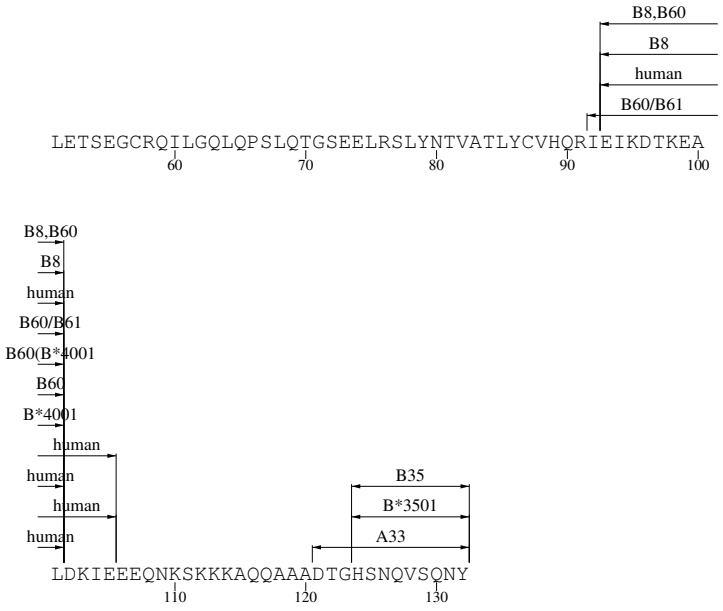
Linear CTL epitopes less than twenty-two amino acids long are shown.

II-C-1 p17 CTL Epitope Map

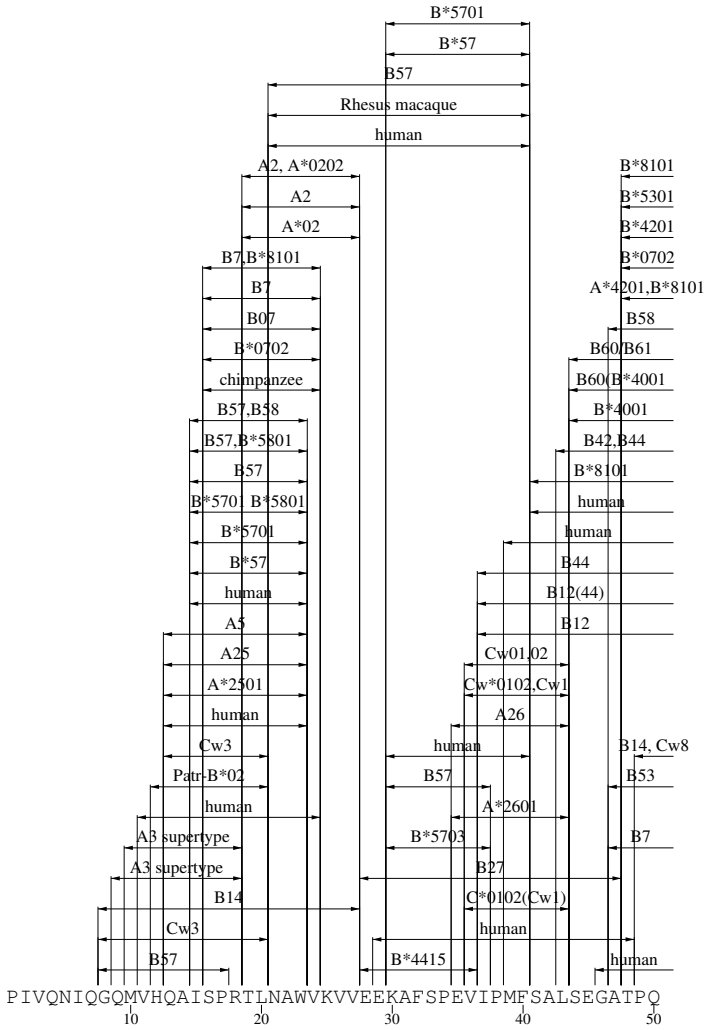


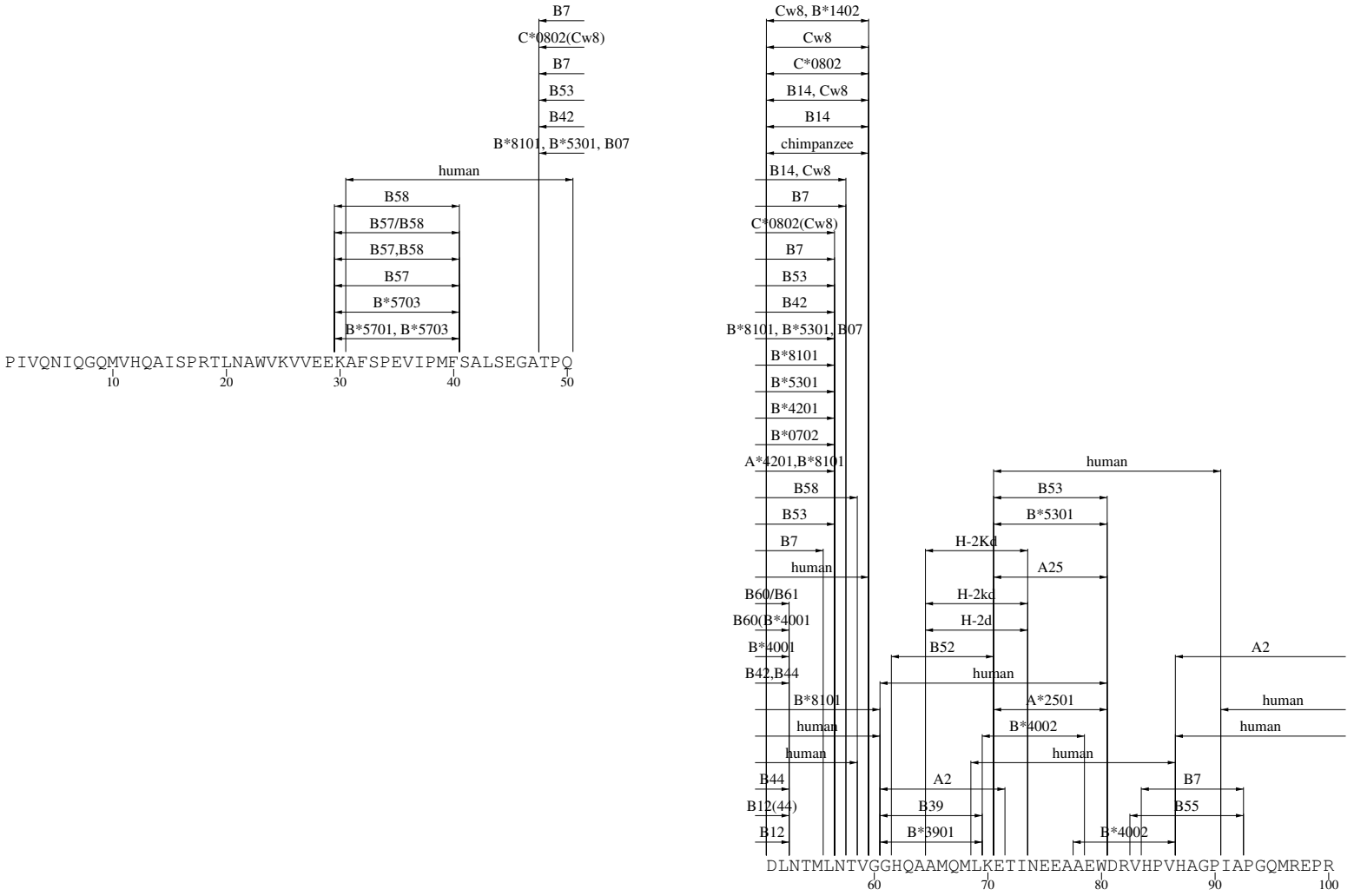

Cw4
A24
A23
A*2402
B8
B8
B*0801
B8
B7
MGARASVLSGGELDRWEKIRLRPGGKKKYKLKHIVWASRELERFAVNPGL
10
20
30
40
50

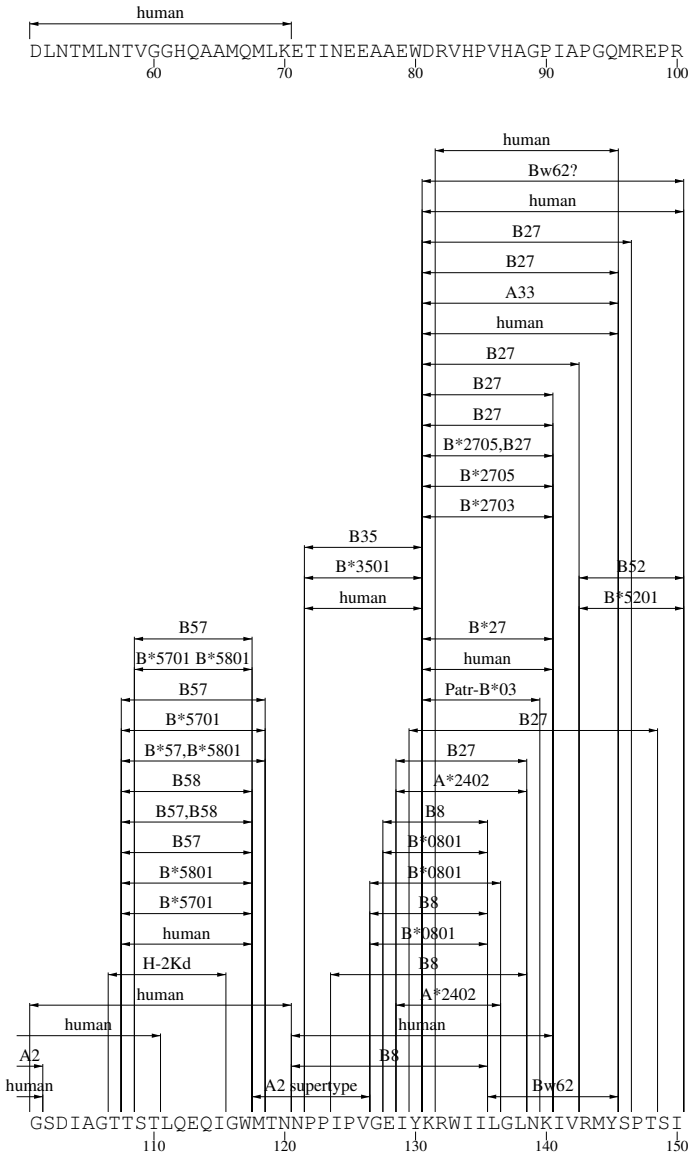

B60(B*4001
B60
human
human
A11
A*1101
A11
A*1101
A11
HLA-A201
B62
B*0201
A2.1
A2, A*0202
A2
A2
A02
A*0214,A*0201
A*0205
A*0202
A*0201
A*0201
A*0201
A*02
human
unknown
A30
A*3002
B8
B*0801
human
A1
B*4001
human
human
LETSEGCRQILGQLQPSLQTGSEELRSLYNTVATLYCVHQRIEIKDTKEA
60
70
80
90
100

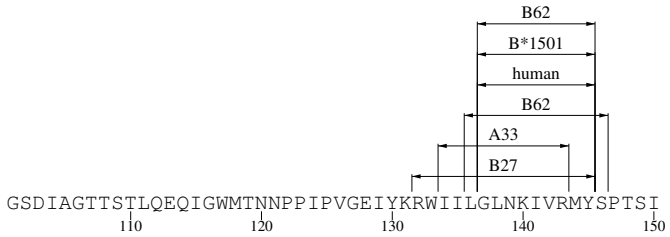


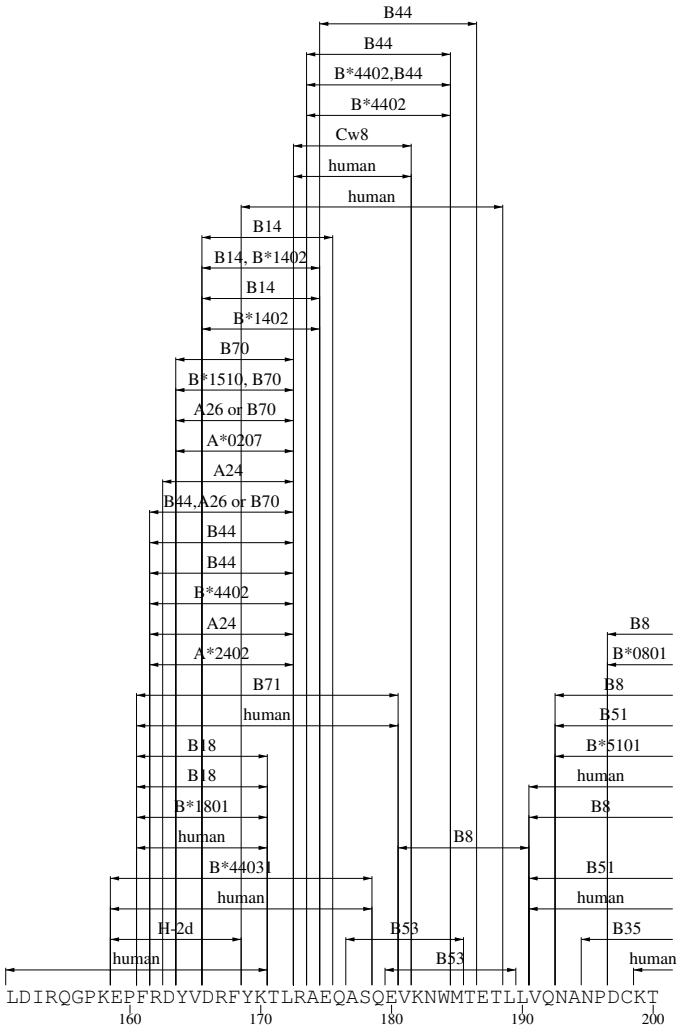
II-C-2 p24 CTL Epitope Map

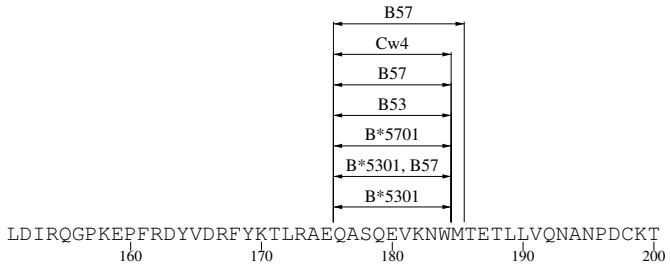


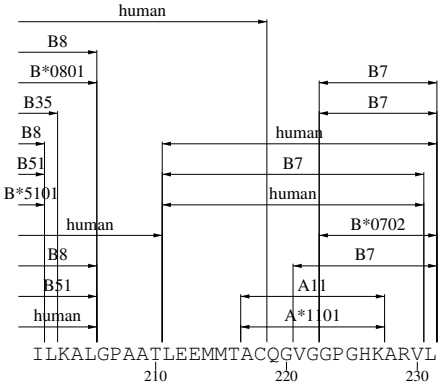

B7
C*0802(Cw8)
B7
B53
B42
B*8101, B*5301, B07
human
B58
B57/B58
B57,B58
B57
B*5703
B*5701, B*5703
PIVQNIQGQMVHQAISPRTLNAWVKVVEEKAFSPEVIPMFSALSEGATPQ
10
20
30
40
50
Cw8, B*1402
Cw8
C*0802
B14, Cw8
B14
chimpanzee
B14, Cw8
B7
C*0802(Cw8)
B7
B53
B42
B*8101, B*5301, B07
B*8101
B*5301
B*4201
B*0702
A*4201,B*8101
B58
B53
B7
human
B60/B61
B60(B*4001
B*4001
B42,B44
B*8101
human
human
B44
B12(44)
B12
human
B53
B*5301
H-2Kd
A25
H-2kd
H-2d
B52
human
A*2501
B*4002
human
A2
B39
B*3901
A2
human
human
B7
B55
B*4002
DLNTMLNTVGGHQAAMQMLKETINEEAAEWDRVHPVHAGPIAPGQMREPR
60
70
80
90
100


human
DLNTMLNTVGGHQAAMQMLKETINEEAAEWDRVHPVHAGPIAPGQMREPR
60
70
80
90
100
human
Bw62?
human
B27
B27
A33
human
B27
B27
B27
B*2705,B27
B*2705
B*2703
B35
B*3501
human
B52
B*5201
B57
B*5701 B*5801
B57
B*5701
B*57,B*5801
B58
B57,B58
B57
B*5801
B*5701
human
H-2Kd
human
human
A2
human
B*27
human
Patr-B*03
B27
B27
A*2402
B8
B*0801
B*0801
B8
B*0801
B8
A*2402
human
B8
A2 supertype
Bw62
GSDIAGTTSTLQEQIGWMTNNPPIPVGEIYKRWIILGLNKIVRMYSPTSI
110
120
130
140
150

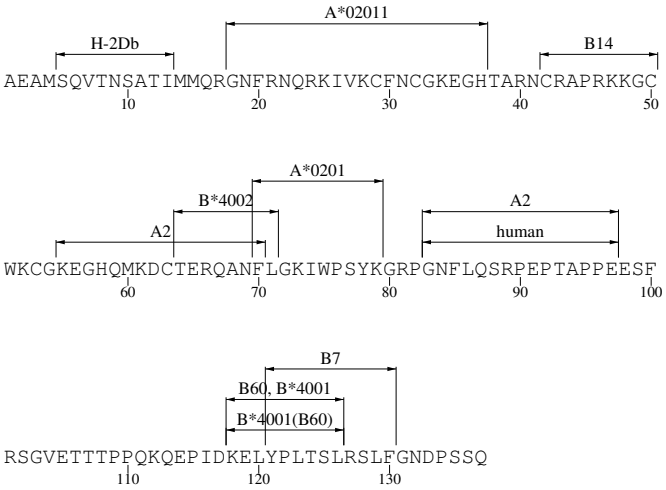

B62
B*1501
human
B62
A33
B27
GSDIAGTTSTLQEQIGWMTNNPPIPVGEIYKRWIILGLNKIVRMYSPTSI
110
120
130
140
150


B44
B44
B*4402,B44
B*4402
Cw8
human
human
B14
B14, B*1402
B14
B*1402
B70
B*1510, B70
A26 or B70
A*0207
A24
B44,A26 or B70
B44
B44
B*4402
A24
A*2402
B71
human
B18
B18
B*1801
human
B*44031
human
H-2d
human
B8
B*0801
B8
B51
B*5101
human
B8
B51
human
B35
human
B8
B53
B53
LDIRQGPKEPFRDYVDRFYKTLRAEQASQEVKNWMTETLLVQNANPDCKT
160
170
180
190
200

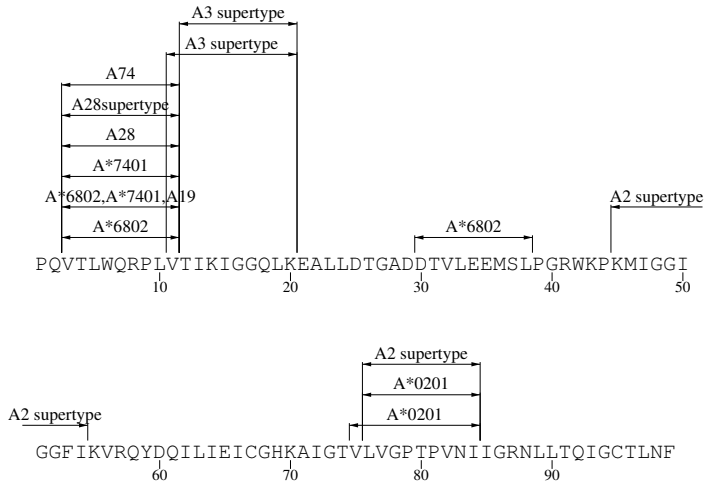

B57
Cw4
B57
B53
B*5701
B*5301, B57
B*5301
LDIRQGPKEPFRDYVDRFYKTLRAEQASQEVKNWMTETLLVQNANPDCKT
160
170
180
190
200


human
B8
B*0801
B35
B8
B51
B*5101
human
B8
B51
human
B7
B7
human
B7
human
B*0702
B7
A11
A*1101
ILKALGPAATLEEMMTACQGVGGPGHKARVL
210
220
230

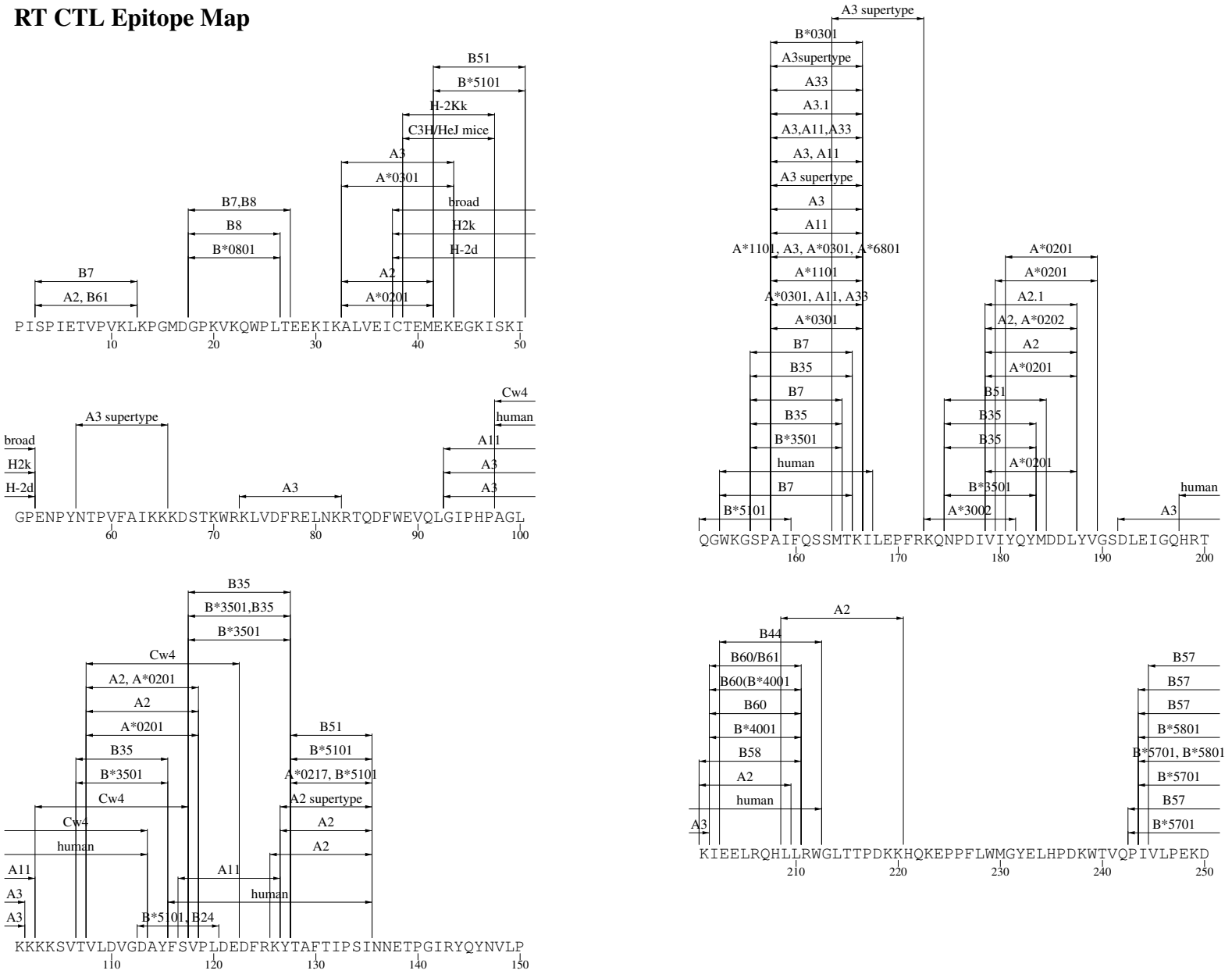
II-C-3 p2p7p1p6 CTL Epitope Map

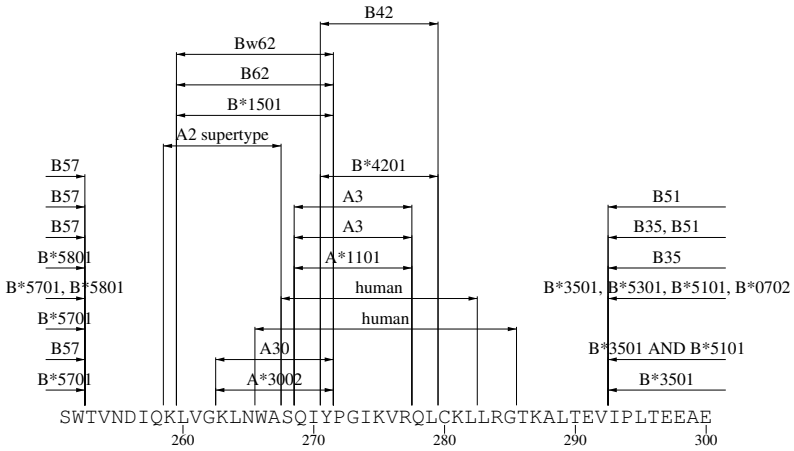


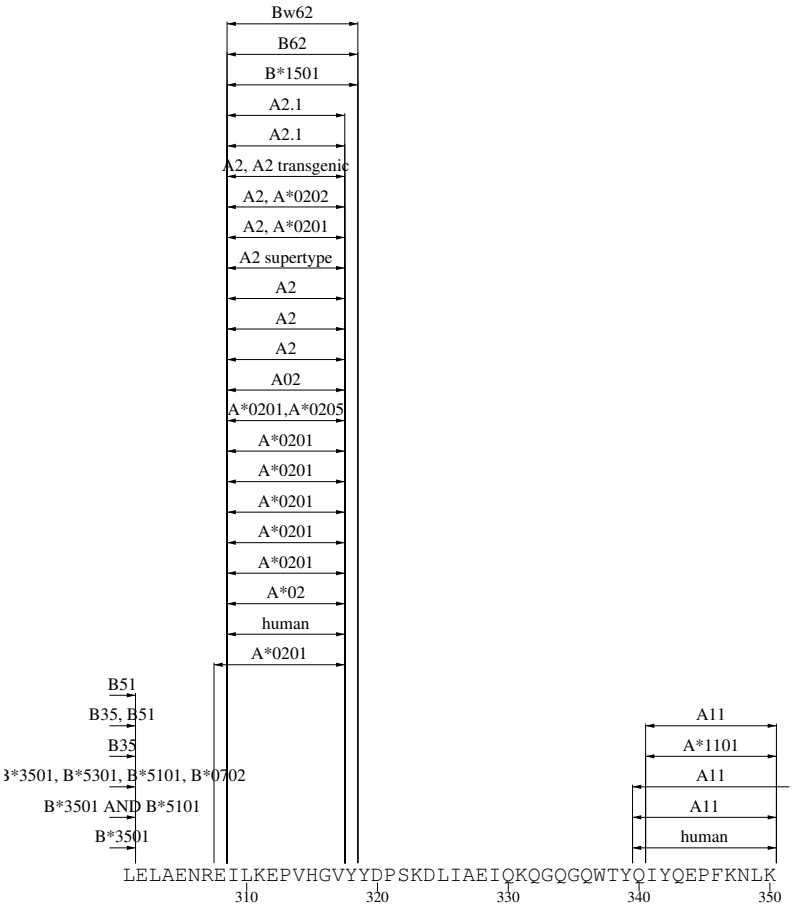
II-C-4 Protease CTL Epitope Map

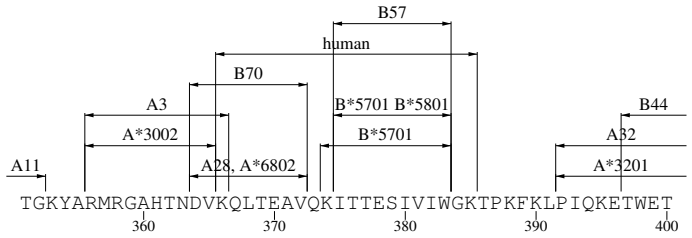


II-C-5 RT CTL Epitope Map

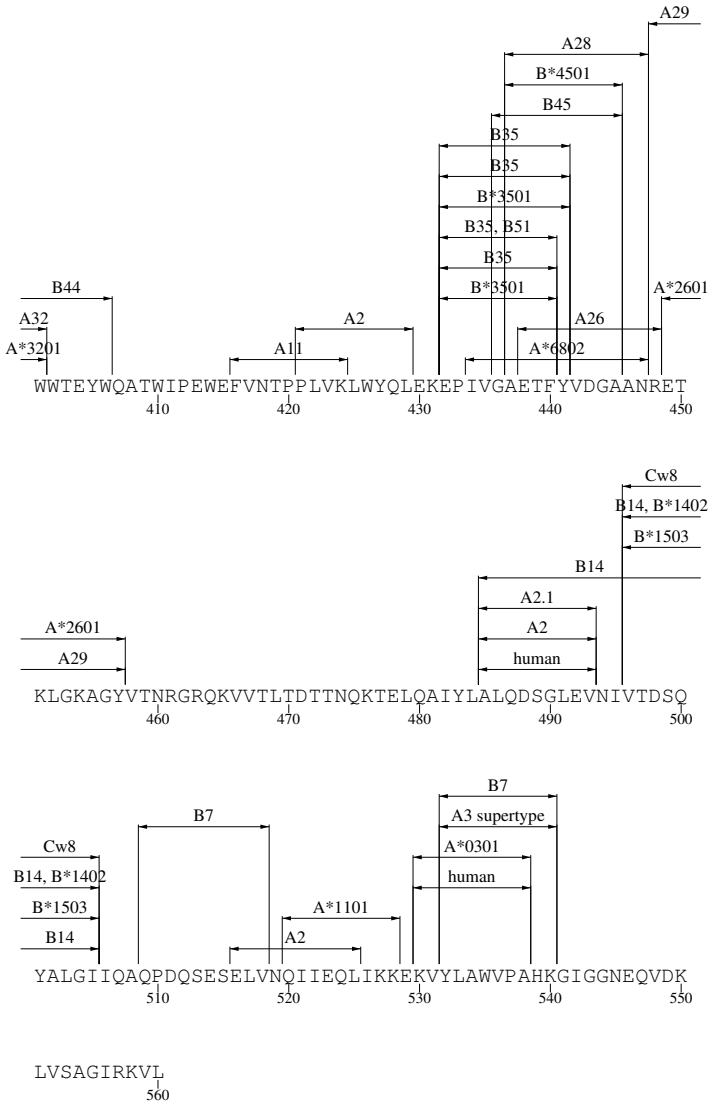



B42
Bw62
B62
B*1501
A2 supertype
B57
B57
B57
B*5801
B*5701, B*5801
B*5701
B57
B*5701
B*4201
A3
A3
A*1101
human
human
A30
A*3002
B51
B35, B51
B35
B*3501, B*5301, B*5101, B*0702
B*3501 AND B*5101
B*3501
SWTVNDIQKLVGKLNWASQIYPGIKVRQLCKLLRGTKALTEVIPLTEEAE
260
270
280
290
300

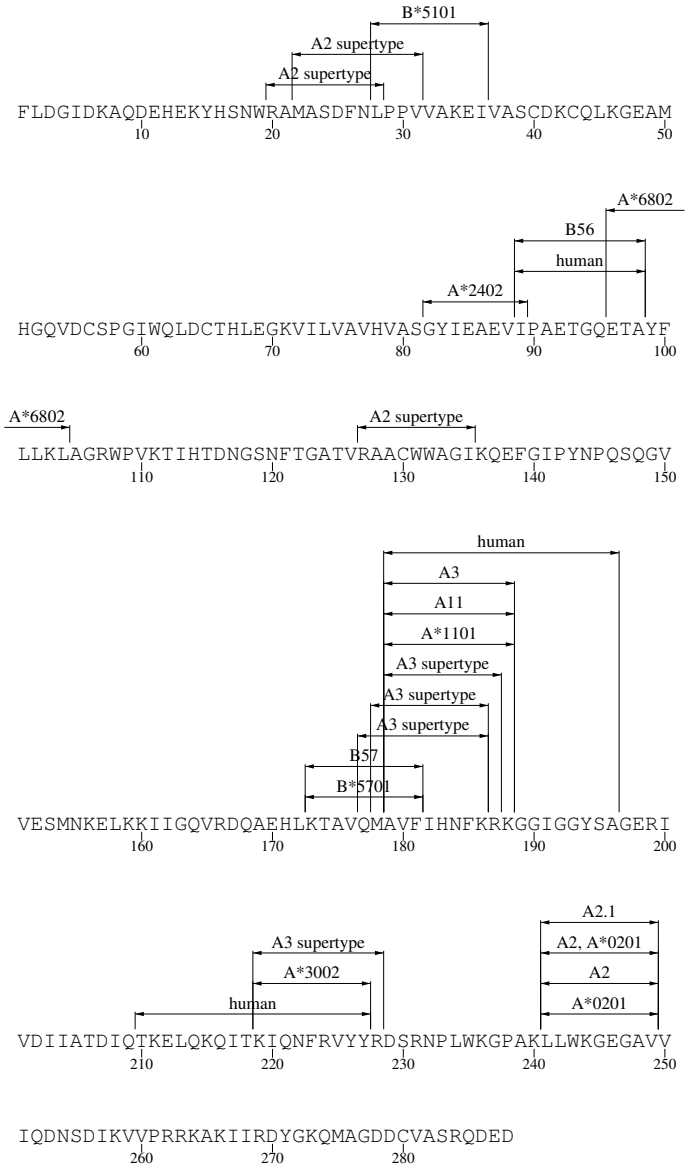

Bw62
B62
B*1501
A2.1
A2.1
A2, A2 transgenic
A2, A*0202
A2, A*0201
A2 supertype
A2
A2
A2
A02
A*0201,A*0205
A*0201
A*0201
A*0201
A*0201
A*0201
A*02
human
A*0201
B51
B35, B51
B35
B*3501, B*5301, B*5101, B*0702
B*3501 AND B*5101
B*3501
A11
A*1101
A11
A11
human
LELAENREILKEPVHGVYYDPSKDLIAEIQKQGQGQWTYQIYQEPFKNLK
310
320
330
340
350


B57
human
B70
A3
A*3002
A11
A28, A*6802
B*5701 B*5801
B*5701
B44
A32
A*3201
TGKYARMRGAHTNDVKQLTEAVQKITTESIVIWGKTPKFKLPIQKETWET
360
370
380
390
400

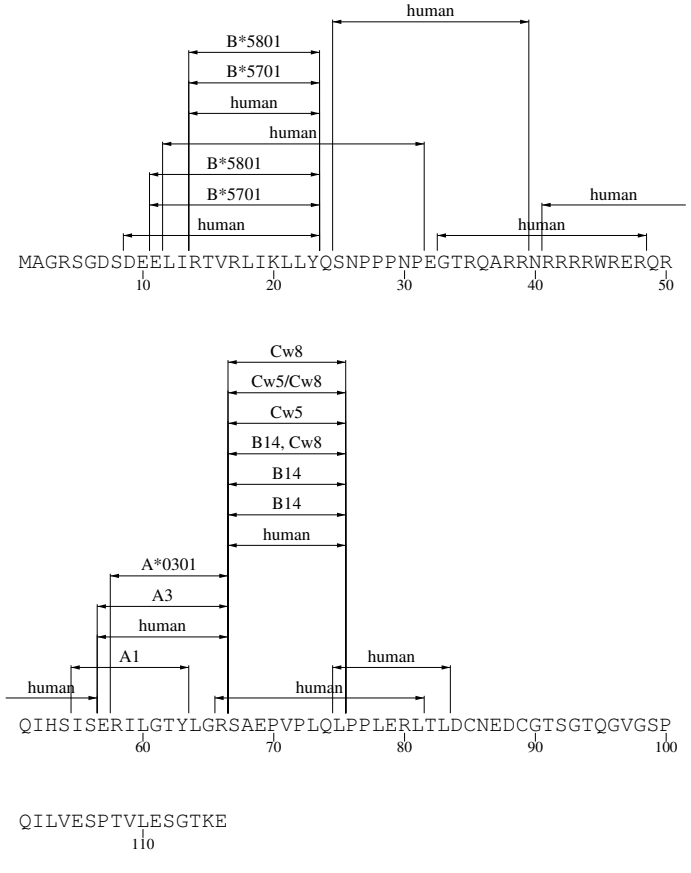
CTL



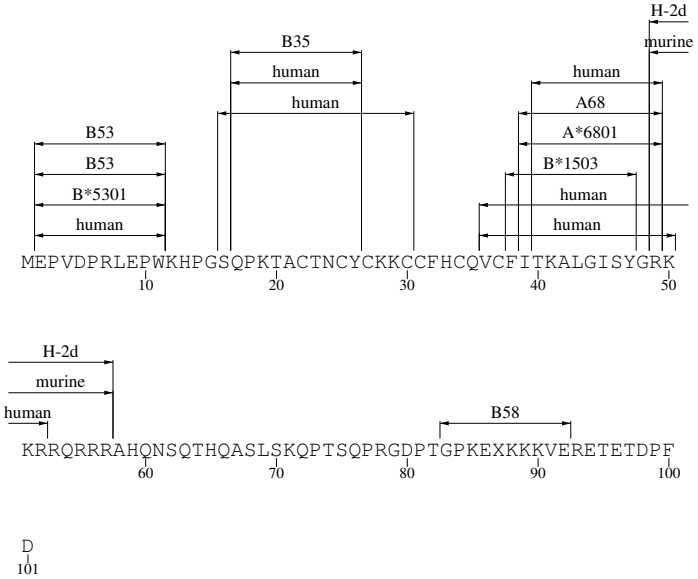
II-C-6 Integrase CTL Epitope Map



II-C-7 Rev CTL Epitope Map

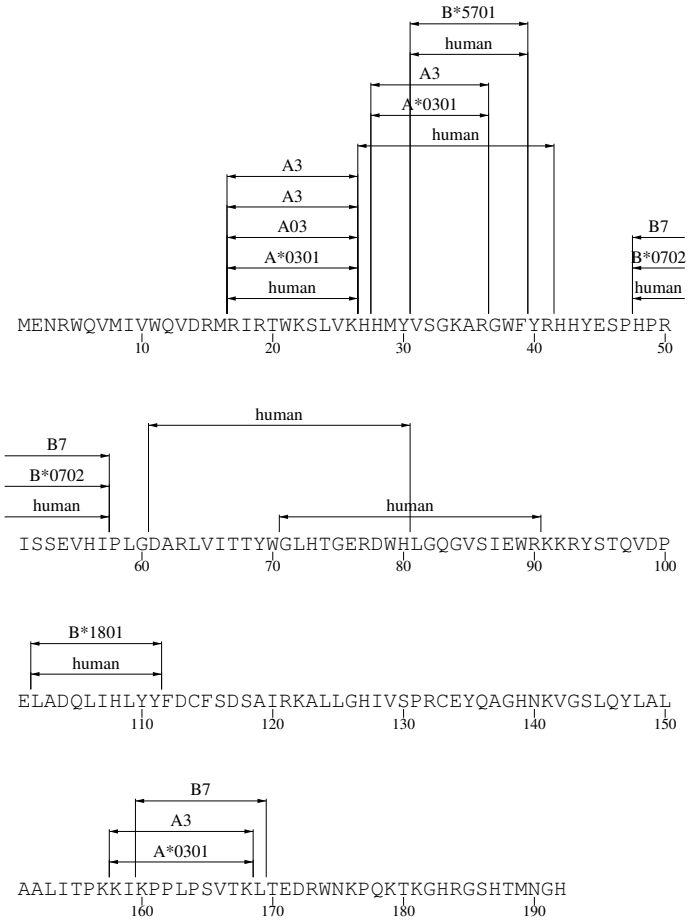


II-C-8 Tat CTL Epitope Map

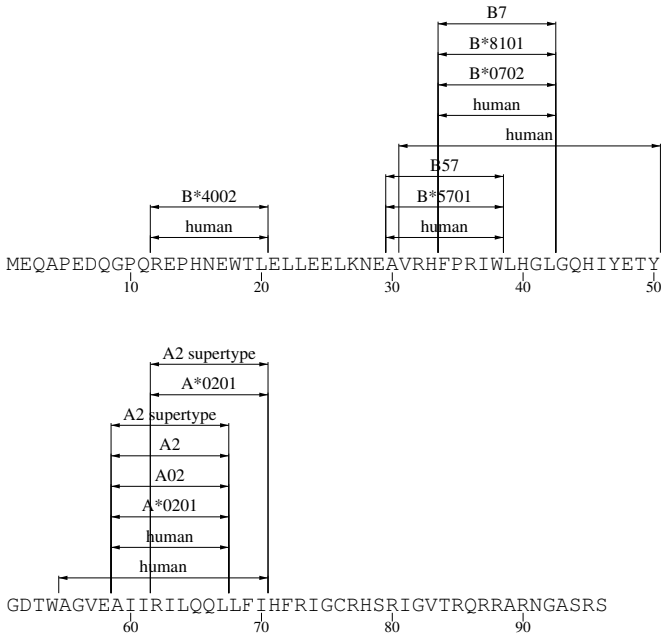


CTL

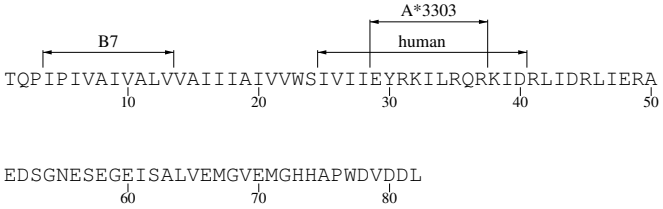
II-C-9 Vif CTL Epitope Map



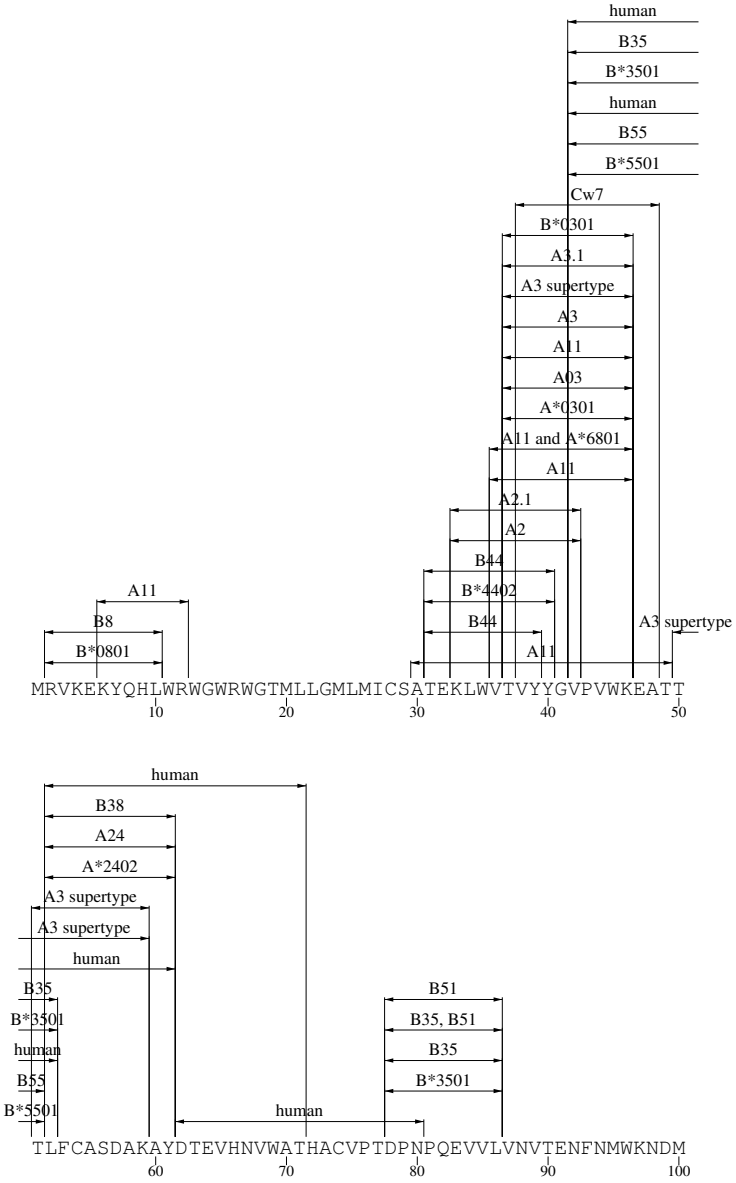
II-C-10 Vpr CTL Epitope Map

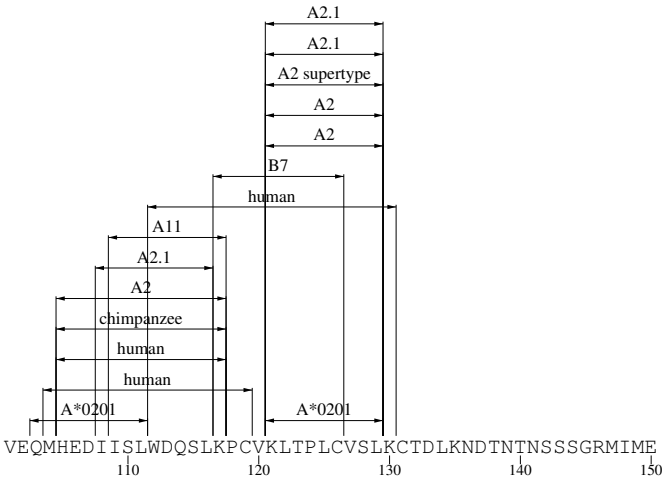


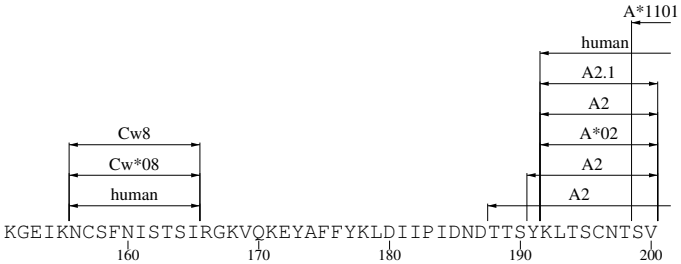
II-C-11 Vpu CTL Epitope Map

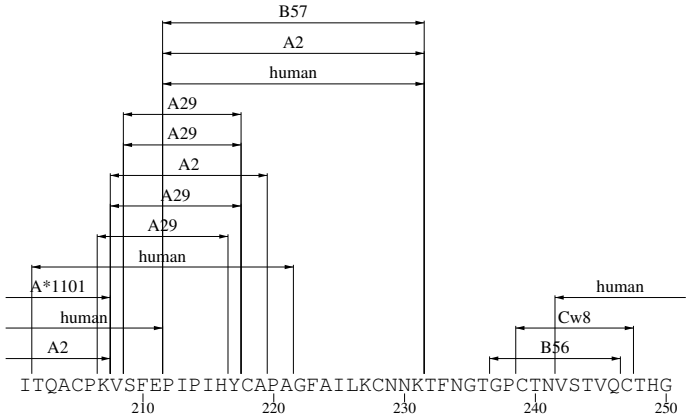


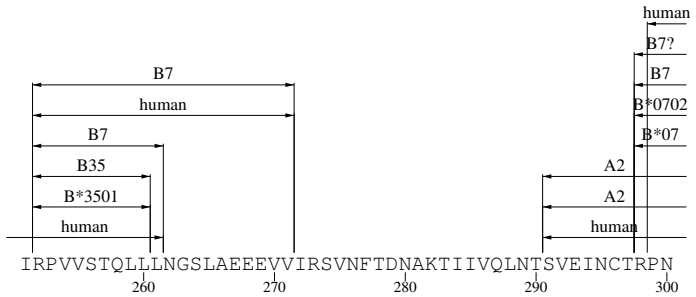
II-C-12 gp160 CTL Epitope Map

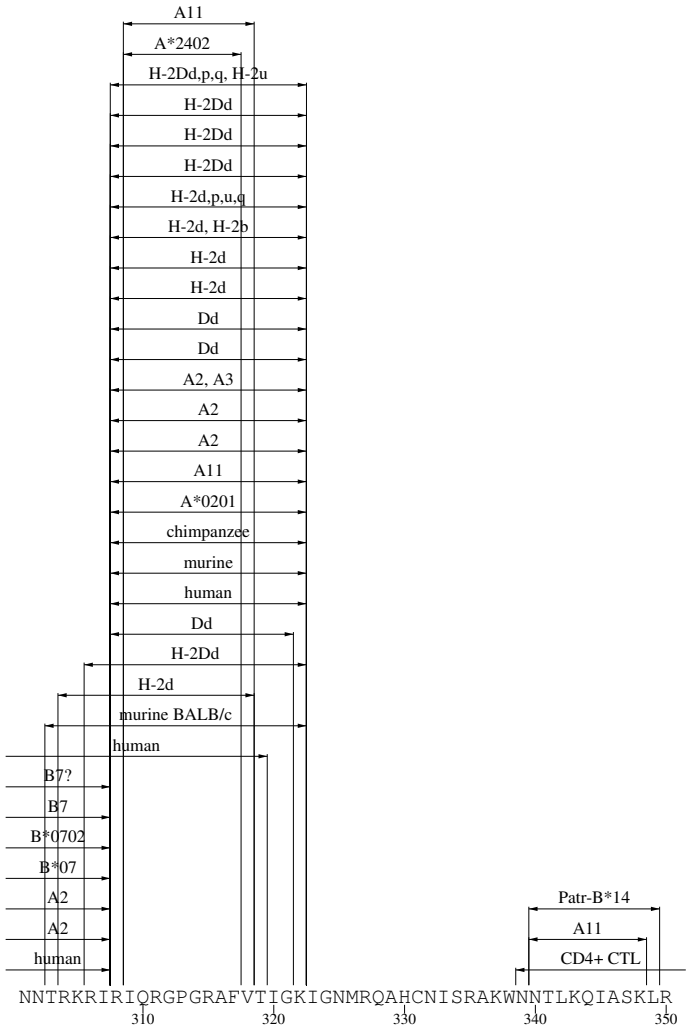


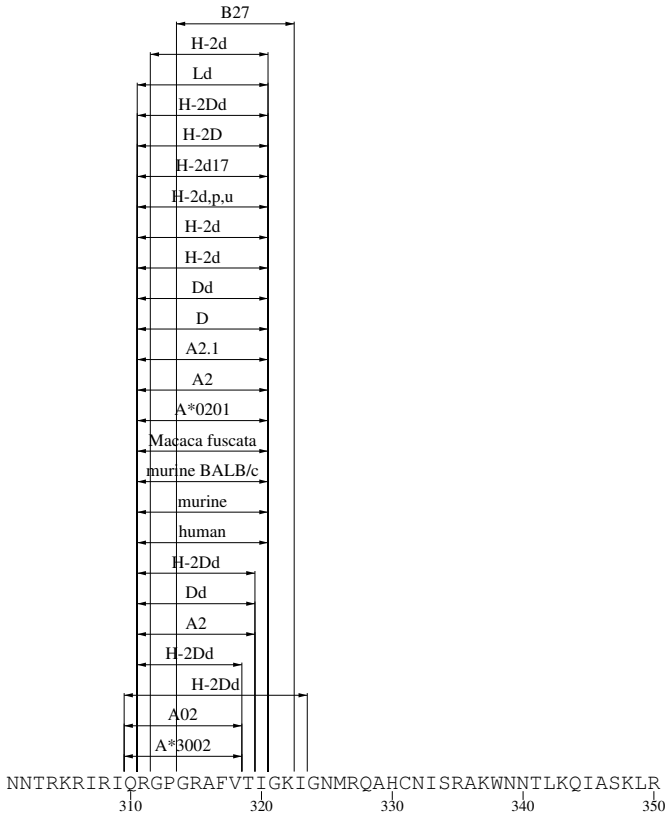

A2.1
A2.1
A2 supertype
A2
A2
B7
human
A11
A2.1
A2
chimpanzee
human
human
A*0201
A*0201
VEQMHEDIISLWDQSLKPCVKLTPLCVSLKCTDLKNDTNTNSSSGRMIME
110
120
130
140
150

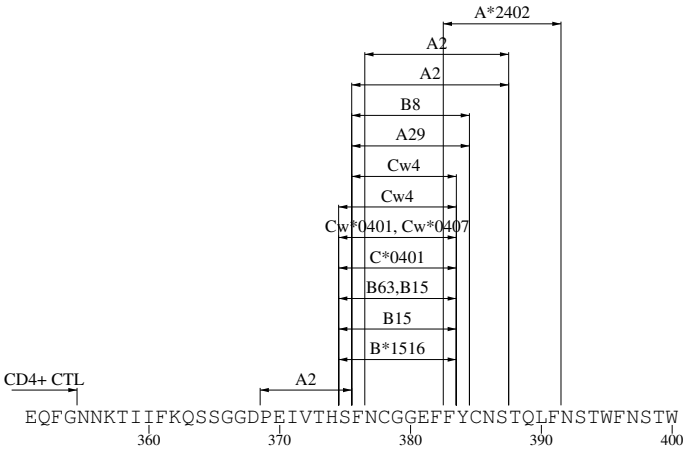

A*1101
human
A2.1
A2
A*02
A2
A2
Cw8
Cw*08
human
KGEIKNCSFNISTSIRGKVQKEYAFFYKLDIIPIDNDTTSYKLTSCNTSV
160
170
180
190
200

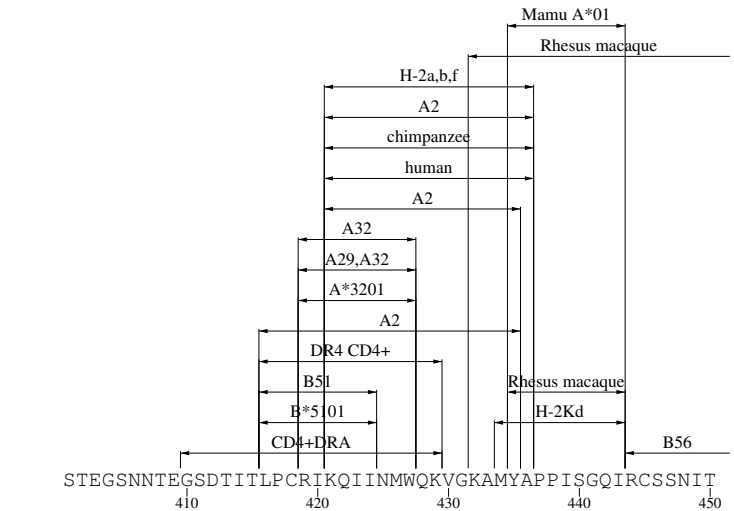

B57
A2
human
A29
A29
A2
A29
A29
human
A*1101
human
A2
human
Cw8
B56
ITQACPKVSFEPIPIHYCAPAGFAILKCNNKTFNGTGPCTNVSTVQCTHG
210
220
230
240
250


human
B7?
B7
B*0702
B*07
B7
human
B7
B35
B*3501
human
A2
A2
human
IRPVVSTQLLLNGSLAEEEVVIRSVNFTDNAKTIIVQLNTSVEINCTRPN
260
270
280
290
300


A11
A*2402
H-2Dd,p,q, H-2u
H-2Dd
H-2Dd
H-2Dd
H-2d,p,u,q
H-2d, H-2b
H-2d
H-2d
Dd
Dd
A2, A3
A2
A2
A11
A*0201
chimpanzee
murine
human
Dd
H-2Dd
H-2d
murine BALB/c
human
B7?
B7
B*0702
B*07
A2
A2
human
Patr-B*14
A11
CD4+ CTL
NNTRKRIRIQRGPGRAFVTIGKIGNMRQAHCNISRAKWNNTLKQIASKLR
310
320
330
340
350

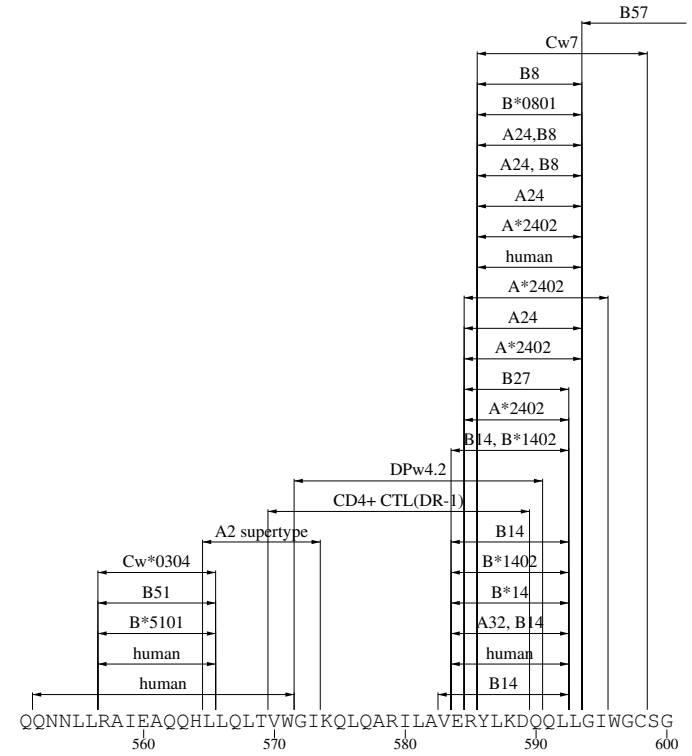

B27
H-2d
Ld
H-2Dd
H-2D
H-2d17
H-2d,p,u
H-2d
H-2d
Dd
D
A2.1
A2
A*0201
Macaca fuscata
murine BALB/c
murine
human
H-2Dd
Dd
A2
H-2Dd
H-2Dd
A02
A*3002
NNTRKRIRIQRGPGRAFVTIGKIGNMRQAHCNISRAKWNNTLKQIASKLR
310
320
330
340
350

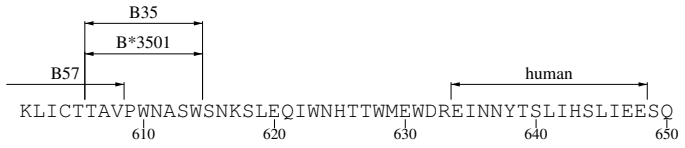

A*2402
A2
A2
B8
A29
Cw4
Cw4
Cw*0401, Cw*0407
C*0401
B63,B15
B15
B*1516
CD4+ CTL
A2
EQFGNNKTIIFKQSSGGDPEIVTHSFNCGGEFFYCNSTQLFNSTWFNSTW
360
370
380
390
400

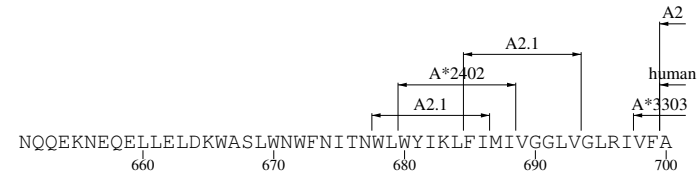

Mamu A*01
Rhesus macaque
H-2a,b,f
A2
chimpanzee
human
A2
A32
A29,A32
A*3201
A2
DR4 CD4+
B51
B*5101
CD4+DRA
Rhesus macaque
H-2Kd
B56
STEGSNNTEGSDTITLPCRIKQIINMWQKVGKAMYAPPISGQIRCSSNIT
410
420
430
440
450

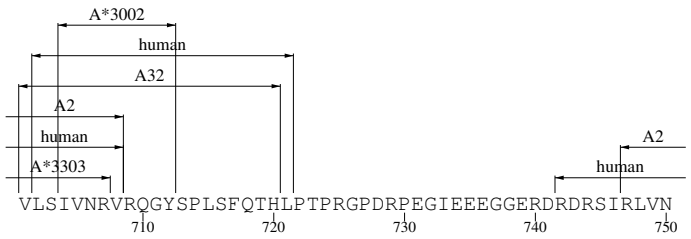

B56
Rhesus macaque
A2
human
GLLLTRDGGNSNNESEIFRPGGGDMRDNWRSELYKYKVVKIEPLGVAPTK
460
470
480
490
500

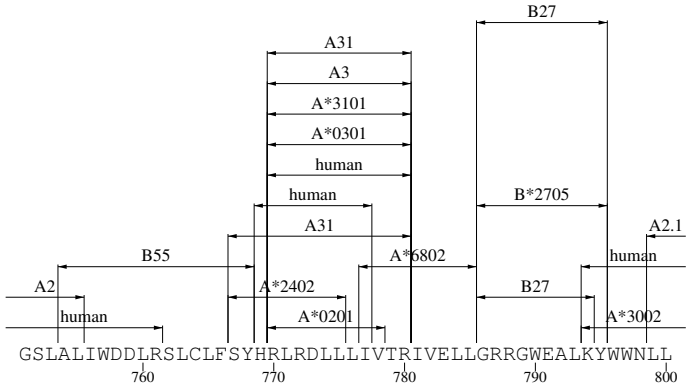

A2
human
AKRRVVQREKRAVGIGALFLGFLGAAGSTMGAASMTLTVQARQLLSGIVQ
510
520
530
540
550

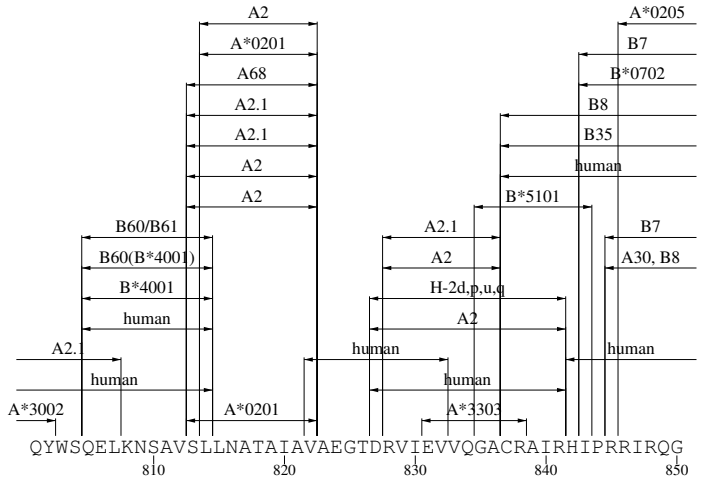

B57
Cw7
B8
B*0801
A24,B8
A24, B8
A24
A*2402
human
A*2402
A24
A*2402
B27
A*2402
B14, B*1402
DPw4.2
CD4+ CTL(DR-1)
A2 supertype
B14
Cw*0304
B*1402
B51
B*14
B*5101
A32, B14
human
human
human
B14
QQNNLLRAIEAQQHLLQLTVWGIKQLQARILAVERYLKDQQLLGIWGCSG
560
570
580
590
600

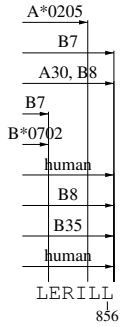

B35
B*3501
B57
human
KLICTTAVPWNASWSNKSLEQIWNHTTWMEWDREINNYTSLIHSLIEESQ
610
620
630
640
650


A2
A2.1
A*2402
human
A2.1
A*3303
NQQEKNEQELLELDKWASLWNWFNITNWLWYIKLFIMIVGGLVGLRIVFA
660
670
680
690
700

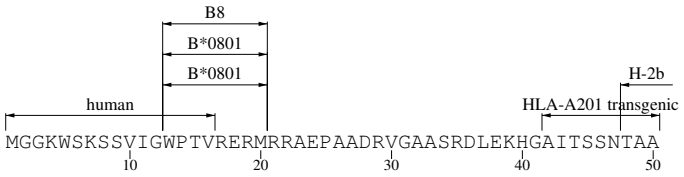

A*3002
human
A32
A2
human
A*3303
A2
human
VLSIVNRVRQGYSPLSFQTHLPTPRGPDRPEGIEEEGGERDRDRSIRLVN
710
720
730
740
750

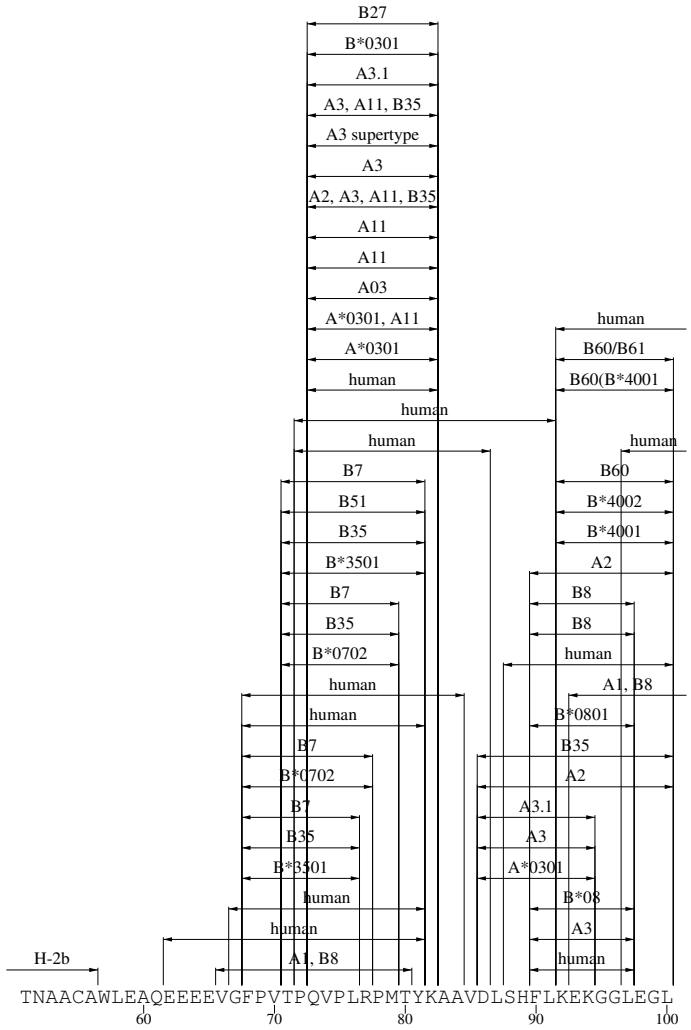

B27
A31
A3
A*3101
A*0301
human
human
B*2705
A31
A2.1
B55
A*6802
human
A2
A*2402
B27
human
A*0201
A*3002
GSLALIWDDLRSLCLFSYHRLRDLLLIVTRIVELLGRRGWEALKYWWNLL
760
770
780
790
800

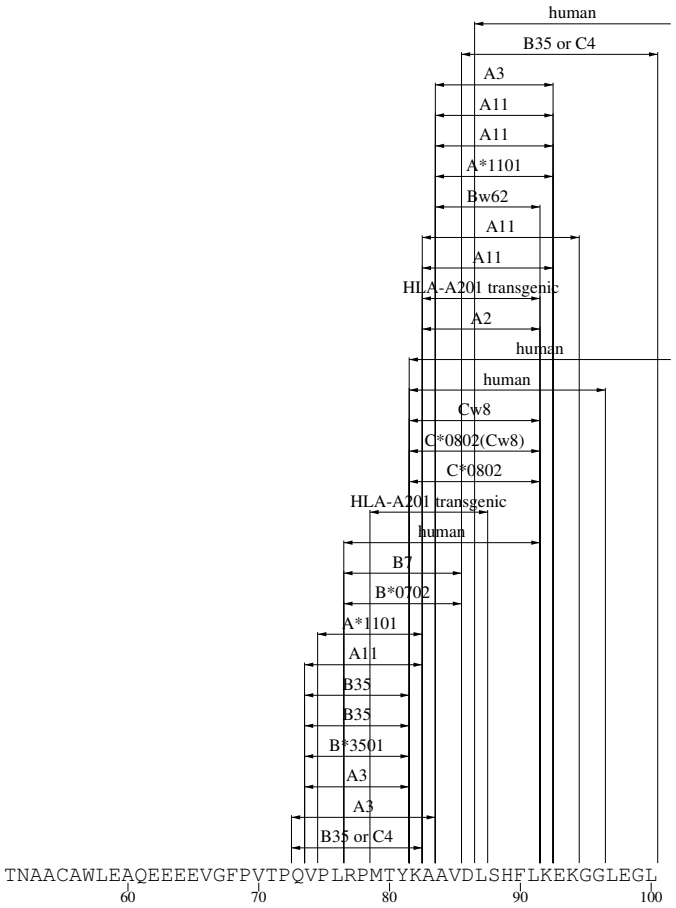

A2
A*0201
A68
A2.1
A2.1
A2
A2
B60/B61
B60(B*4001)
B*4001
human
A2.1
human
A*3002
A*0201
A*0205
B7
B*0702
B8
B35
human
B*5101
A2.1
A2
H-2d,p.u,q
A2
human
human
human
A*3303
B7
A30, B8
QYWSQELKNSAVSLLNATAIAVAEGTDRVIEVVQGACRAIRHIPRRIRQG
810
820
830
840
850

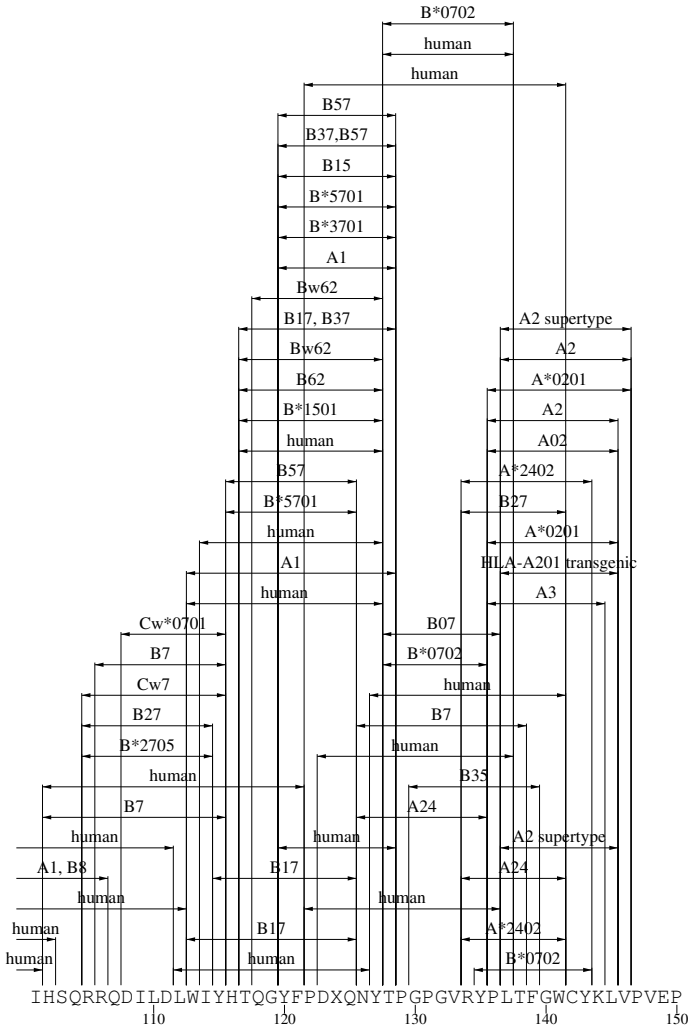

A*0205
B7
A30, B8
B7
B*0702
human
B8
B35
human
LERILL
856

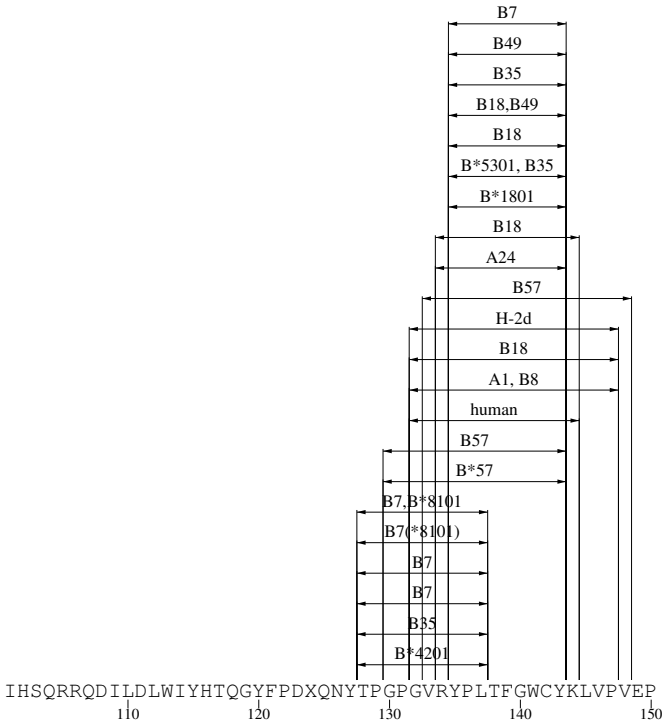
II-C-13 Nef CTL Epitope Map

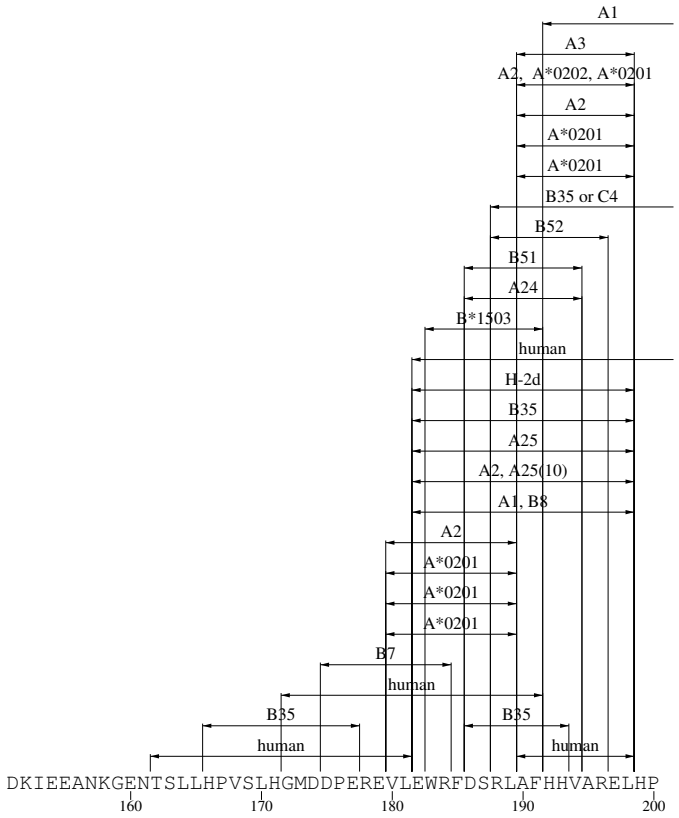


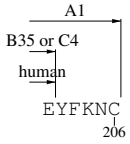



human
B35 or C4
A3
A11
A11
A*1101
Bw62
A11
A11
HLA-A201 transgenic
A2
human
human
Cw8
C*0802(Cw8)
C*0802
HLA-A201 transgenic
human
B7
B*0702
A*1101
A11
B35
B35
B*3501
A3
A3
B35 or C4
TNAACAWLEAQEEEEVGFPVTPQVPLRPMTYKAAVDLSHFLKEKGGLEGL
60
70
80
90
100


B*0702
human
human
B57
B37,B57
B15
B*5701
B*3701
A1
Bw62
B17, B37
Bw62
B62
B*1501
human
B57
B*5701
human
A1
human
Cw*0701
B7
Cw7
B27
B*2705
human
B7
human
A1, B8
human
human
B17
B17
human
human
A2 supertype
A2
A*0201
A2
A02
A*2402
B27
A*0201
HLA-A201 transgenic
A3
B07
B*0702
human
B7
A24
human
A2 supertype
B17
A24
human
A*2402
B*0702
IHSQRRQDILDLWIYHTQGYFPDXQNYTPGPGVRYPLTFGWCYKLVPVEP
110
120
130
140
150


B7
B49
B35
B18,B49
B18
B*5301, B35
B*1801
B18
A24
B57
H-2d
B18
A1, B8
human
B57
B*57
B7,B*8101
B7(*8101)
B7
B7
B35
B*4201
IHSQRRQDILDLWIYHTQGYFPDXQNYTPGPGVRYPLTFGWCYKLVPVEP
110
120
130
140
150


A1
A3
A2, A*0202, A*0201
A2
A*0201
A*0201
B35 or C4
B52
B51
A24
B*1503
human
H-2d
B35
A25
A2, A25(10)
A1, B8
A2
A*0201
A*0201
A*0201
B7
human
B35
B35
human
human
DKIEEANKGENTSLLHPVSLHGMDDPEREVLEWRFDSRLAFHHVARELHP
160
170
180
190
200


A1
B35 or C4
human
EYFKNC
206

Part III

HIV Helper T-Cell Epitopes

III-A Summary

Part III includes tables and maps of HIV-specific helper T-cell (Th) epitopes arranged sequentially according to the location of the proteins in the HIV-1 genome. This section parallels the organization of the CTL section. We attempted to make this section as comprehensive as possible, requiring that the epitope be contained within a region of 30 amino acids maximum, but not that the precise boundaries be defined. The HLA specificity is usually not determined for Th epitopes. For more recent updates, epitope sequence alignments, and useful searching capabilities, please see our web site: `http://hiv-web.lanl.gov/immunology`. The same epitope can have multiple entries, as each entry represents a single publication. Helper T-cell responses to proteins with no defined epitope are described at the end of each protein section.

Recent studies utilize multiple functions attributed to T cells to define responses, and the simple distinctions of cytotoxic T-cell and helper T-cells have become blurred as more is learned about the range of responses triggered in CD4 and CD8 positive T-cells responding to antigenic stimulus. When adding the most recent studies to the database, we have tried to place T cell responses in a reasonable manner into our traditional helper T cell and CTL sections, and to specify the assay used to measure the response in each study.

III-A-1 Tables

Each Th epitope has a six-part basic entry:

HXB2 Location: The viral strain HXB2 (GenBank Accession Number K03455) is used as a reference strain throughout this publication. The position of the defined epitope location relative to the sequence of the HXB2 protein is indicated. The numbering in this table corresponds to the protein maps. Because of HIV-1 variation the epitope may not actually be present in HXB2, rather the position in HXB2 indicates the position aligned to the epitope. HXB2 was selected as the reference strain because so many studies use HXB2, and because crystal structures for HXB2-related proteins are often available. The precise positions of an epitope on the HXB2 reference strain can be readily obtained using the interactive position locator at our web site: `http://hiv-web.lanl.gov/content/hiv-db/LOCATE_SEQ/locate.html`.

Author Location: The amino acid positions of the epitope boundaries and the reference sequence are listed as given in the primary publication. Frequently, these positions as published are imprecise, and do not truly correspond to the numbering of the sequence, but they provide a reasonable guide to the peptide's approximate location in the protein. Also, in many cases the reference sequence identification was not provided, and in such cases it is not possible to use these numbers to specify precise locations.

Epitope Sequence: The amino acid sequence of the epitope of interest as defined in the reference, based on the reference strain used in the study defining the epitope. On occasions when only the position numbers and not the actual peptide sequence was specified in the original publication, we tried to fill in the peptide sequence based on the position numbers and reference strain. If the sequences were numbered inaccurately by the primary authors, or if we made a mistake in this process, we may have misrepresented the binding site's amino acid sequence. Because of this uncertainty, epitopes that were not explicitly written in the primary publication, that we determined by looking up the reference strain and the numbered location, are followed by a question mark in the table.

Immunogen: The antigenic stimulus of the Th response to the defined epitope. Often this is an HIV-1 infection. If a vaccine was used as the original antigenic stimulation, not a natural infection, this is noted on a separate line, and additional information about the vaccine antigen is provided as available.

Species(HLA): The species responding and HLA specificity of the epitope, when known.

Reference: The primary reference (sometimes two or more directly related studies are included). Details for some of the earlier references are in Part V.

Following the entry for a given Th epitope are brief comments explaining the context in which the epitope was studied and what was learned about the epitope in a given study.

III-A-2 HIV Protein Epitope Maps

All HIV Th epitopes mapped to within a region of 21 amino acids or less are indicated on the HIV protein epitope maps. The location and HLA restriction elements of Th epitopes are indicated on protein sequences of HXB2. These maps are meant to provide the relative location of defined epitopes on a given protein, but the HXB2 sequence may not actually carry the epitope of interest, as it may vary relative to the sequence for which the epitope was defined. Epitopes with identical boundaries and HLA fields are included in the maps only once. If one laboratory determines HLA presenting molecules at the serotype level (example: A2) and another at the genotype level (example: A*0201) both will be included in the map. MHC specificities are indicative of the host species; when no MHC presenting molecule is defined, the host species is noted.

III-A-3 Alignments

To conserve space, no epitope alignments are provided in this book, but they can be generated using the T helper epitope search tool at `http://hiv-web.lanl.gov/immunology`. All epitopes are aligned to the HXB2 sequence, with the sequence used to define the epitope indicated directly above it. Sequences are sorted by their subtype and country of origin.

The master alignment files from which the epitope alignments were created are available at our web site (`http://hiv-web.lanl.gov/ALIGN_CURRENT/ALIGN-INDEX.html`). The alignments were modified in some cases to optimize the alignment relative to the defined epitope and minimize insertions and deletions; epitope alignments are generated by anchoring on the C-terminal residue. A dash indicates identity to the consensus sequence, and a period indicates an insertion made to maintain the alignment. Stop codons are indicated with a `$`, and frameshifts by a `#`, or ambiguous codons (nucleotide was `r`, `y`, or `n`) by an `x`; they are inserted to maintain the alignments. In consensus sequences an upper case letter indicates the amino acid was present in all sequences, a lower case letter indicates the amino acid was present in most sequences in a given position, and a question mark indicates two or more amino acids were represented with equal frequency.

III-B HIV Helper T-Cell Epitope Tables

All HIV Helper T-Cell epitopes arranged by protein position. The table entries are sorted in a nested way—first by protein, then by HXB2 start location within the protein and finally by HLA presenting molecule. Epitopes for which the HXB2 location is unknown appear at the end of the listing of the protein in which they are located.

III-B-1 p17 Helper T-Cell Epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17 (18–42)	p17 (18–42 PV22)	KIRLRPGGKKKYKLKHIVW-ASRELE	HIV-1 infection	human (DRB1*13)	Lotti2002
	• 10/49 chronically HIV-1 infected patients had low p55-Gag-specific CD4+ T cell responses prior to therapy, and these responses remained unchanged 3 and 6 months after initiation of HAART. There was no difference in level of response in those with or without a detectable p55 response. • For one individual, patient F45 CDC stage A2, CD4+ p55 responding clones were generated. Her response was consistently strong and heterogeneous in terms of HLA restriction and Vbeta usage, and some clones had a Th1 cytokine secretion profile (high IFNgamma production) while some had a Th2 profile (high IL-4 and IL-5 production). 5/10 CD4+ clones could also induce cytotoxicity. • 4/10 clones from patient F45 had their epitopes mapped using overlapping peptides. Clone 6 recognized this peptide sequence restricted by DRB1*13. This clone had a high SI (27.1 to p55, 90.6 to peptide) secreted IFNgamma, indicative of a Th1 response, as well as TNFalpha. Clone 6 was highly cytotoxic, through a perforin-mediated pathway.			
p17 (21–35)	p17 (21–35 SF2)	LRPGGKKKYKLKHIV	HIV-1 infection	human (DR13.02)	Harcourt1998
	• 43 asymptomatic HIV+ individuals were screened for proliferative responses to HIV – 12 showed a response, and dominant epitopes were mapped for two individuals, one in p24 and one in p17 • Patient 024's naturally occurring variant LRPGGKKKYQLKHIV also elicited a strong proliferative response. • Naturally occurring variants of this epitope were found within the individual who made this response – several did not stimulate the CD4+ T-cell line that recognized the index peptide, suggestive of immune escape				
p17 (22–29)	p17 (22–29 LAI)	RPGGKKKY?	HIV-1 infection	human	Schrier1989
	• Stimulates T-cell proliferation in HIV-infected donors. • Schrier lists this peptide as p24(22-29), but it appears to be in p17.				
p17 (33–47)	p17 (33–47 IIIB, B10)	HIVWASRELERFAVN?	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• Peptides were identified that commonly evoke T-cell responses – 57% of 90 HIV+ people had a T-cell response to this peptide				
p17 (35–59)	p17 (35–49 PV22)	VWASRELERFAVNPGLLET-SEGCRQ	HIV-1 infection	human (DRB1*13)	Lotti2002
	• 10/49 chronically HIV-1 infected patients had low p55-Gag-specific CD4+ T cell responses prior to therapy, and these responses remained unchanged 3 and 6 months after initiation of HAART. There was no difference in level of response in those with or without a detectable p55 response. • For one individual, patient F45 CDC stage A2, CD4+ p55 responding clones were generated. Her response was consistently strong and heterogeneous in terms of HLA restriction and Vbeta usage, and some clones had a Th1 cytokine secretion profile (high IFNgamma production) while some had a Th2 profile (high IL-4 and IL-5 production). 5/10 CD4+ clones could also induce cytotoxicity.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• 4/10 clones from patient F45 had their epitopes mapped using overlapping peptides. Clone 25 recognized this peptide sequence restricted by DRB1*13 using TCR Vbeta 5.1. This clone had a SI of 4.9 to p55, 13.7 to peptide, secreted low levels of IFNgamma, indicative of a Th1 response. Clone 25 had cytotoxic activity, mediated through both a perforin and a Fas-based pathway.				
p17 (93–107)	p17 (93–107 IIIB, B10)	EIKDTKEALDKIEEE	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				
p17 (118–132)	p17 (118–132 IIIB, B10)	AAADTGHSSQVSQNY	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				

III-B-2 p24 Helper T-Cell Epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (1–11)	p24 (1–11 SF2)	PIVQNLQGQMV	HIV-1 infection	human (DR1)	Harcourt1998
	• 43 asymptomatic HIV+ individuals were screened for proliferative responses to HIV – 12 showed a response, and dominant epitopes were mapped for two individuals, one in p24 and one in p17 • Out of five truncated versions of peptide PIVQNLQGQMVHQAISPRTL, only p24(1-11) elicited a proliferative response • Nine naturally occurring variants of this epitope were found within the individual who made this response – all bound to HLA-DR1, but three did not stimulate the CD4+ T-cell line that recognized the index peptide, suggestive of immune escape				
p24 (1–15)	p24 (133–147 IIIB, B10)	PIVQNIQGQMVHQAI	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• Peptides were identified that commonly evoke T-cell responses – 62% of 90 HIV+ people had a T-cell response to this peptide				
p24 (1–22)	p24 (133–154 SF2)	PIVQNIQGQMVHQAISPRT-LNA	HIV-1 infection	human	Rosenberg1997
	• While anti-HIV CD4 Th responses are characteristically undetectable in chronic infections, strong p24-specific proliferative responses were inversely correlated with low viral load in 10 chronically infected people • The dominant proliferative response in one of two long term survivors was to this peptide				
p24 (7–21)	Gag (171–185)	QGQMVHQAISPRTLN	HIV-1 infection	human (DR supermotif)	Wilson2001
	• Epitope name: Gag 171 • Eleven peptides were identified that had the HLA-DR supermotif, all were found to bind to MHC class II DR molecules and all elicited proliferative responses from multiple HIV-infected donors • This epitope binds to nine HLA-DR alleles: DRB1*0101, DRB1*1501, DRB1*0401, DRBI*0405, DRB1*1302, DRB1*0701, DRB1*0901, DRB5*0101 and DRB4*0101 with an IC_{50} threshold below 1,000 nM • This epitope sequence is conserved in 52% of clade B isolates • 7/22 HIV infected individuals responded to this epitope (13/22 responded to some of the DR supermotif epitopes, the 9 non-responder peptides tended to also not have recall responses to rec HIV-1 whole proteins)				
p24 (7–21)	Gag (171–185)	QGQMVHQAISPRTLN	Vaccine	murine (I-Ab and HLA-DR)	Livingston2002
	Vaccine *Vector/Type:* DNA with CMV promotor, peptide *HIV component:* polyepitope *Adjuvant:* CFA • Epitope name: Gag 171 • Four Th HIV epitopes presented by HLA-DR molecules were identified that also could be presented my murine class II molecule I-Ab, enabling testing of vaccine strategies of in H-2b mice. • Responses to pooled peptides, polyepitope peptides in a linear construct or in a branched MAP construct, and a DNA polyepitope construct with a CMV promotor were compared. A linear arrangement in polyepitope construct created a junctional epitope that could be disrupted with the addition of GPGPG spacers. The linear polyepitope construct with the GPGPG spacer worked well in terms of eliciting responses to all four peptides, using either DNA or protein for the vaccination.				
p24 (11–26)	p24 (143–157)	VHQAISPRTLNAWVKC	in vitro stimulation	human	Bedford1997
	• Epitope elicits a primary proliferative response in PBMC from uninfected donors • Matches 3/3 anchor residues for HLA DR: **V**HQAI**S**PR**T**				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (11–30)	Gag (143–152 SF2)	VHQAISPRTLNAWVKVVEEK	Vaccine	murine (H-2^d, H-2^b)	Mata1999
	Vaccine *Vector/Type:* Listeria moncytogenes *Strain:* SF2 *HIV component:* p24 • Listeria moncytogenes is an intracellular bacterium that lives in the cytoplasm and generates a cell-mediated immune response • Listeria moncytogenes vaccine expressing HIV-1 p24 protein (Lm-Gag) was used to stimulate gag specific CD4+ T cell proliferative responses in BALB/c(H-2d) and C57BL/6(H-2b) mice • Two of three reactive p24 peptides (out of 22 overlapping peptides that span p24) were recognized by both murine strains – this epitope is immunodominant in C57BL/6 mice and also can stimulate a BALB/c response • The proliferative response is due to CD4+, IFN-gamma producing cells, a Th1 response				
p24 (11–30)	p24 (143–162 HXB2)	VHQAISPRTLNAWVKVVEEK	Vaccine	murine (H-2^d, H-2^b)	Mata1999
	Vaccine *Vector/Type:* Listeria monocytogenes *Strain:* HXB2 *HIV component:* Gag • BALB/c and C57BL/6 mice were immunized with rec Listeria monocytogenes (Lm-Gag) expressing HIV-1 HXB2 Gag • L. monocytogenes is a gram-positive bacteria that enters the macrophage on phagocytosis and lives in the cytoplasm – secreted L. monocytogenes antigens are processed and presented by both class I and class II pathways • The class II T helper response was probed using 20 mer peptides that overlapped by 10, and the peptides VHQAISPRTLNAWVKVVEEK and FRDYVDRFYKTLRAEQASQD were recognized in H-2^b and H-2^d mice				
p24 (21–36)	p24 (153–167)	NAWVKVVEEKAFSPEC	in vitro stimulation	human	Bedford1997
	• Epitope elicits a primary proliferative response in PBMC from uninfected donors				
p24 (31–46)	p24 (163–177)	AFSPEVIPMFSALSEC	in vitro stimulation	human (A*0201)	Bedford1997
	• E elicits a primary proliferative response in PBMC from uninfected donors • Peptide contains a CTL epitope identified in HIV-positive patients • Peptide binds to HLA A*0201 and causes regulation of class I expression on T2 cells • Matches 3/3 anchor residues for HLA DR: **V**IPMF**S**AL**S**				
p24 (31–52)	p24 (163–184 SF2)	AFSPEVIPMFSALSEGATP-QDL	HIV-1 infection	human	Rosenberg1997
	• Low viral load correlated with strong HIV-1-specific proliferative response • A proliferative response to this epitope was detected in two long term survivors				
p24 (41–56)	p24 (173–187)	SALSEGATPQDLNTMC	in vitro stimulation	human	Bedford1997
	• Epitope elicits a primary proliferative response in PBMC from uninfected donors				
p24 (48–62)	p24 (180–194)	TPQDLNTMLNTVGGH	HIV-1 infection	human	Adams1997
	• One of four immunogenic Gag peptides used in study of proliferative response to p24 • Homology to an SIV epitope recognized by macaque T-cells • T-cells from 8 of 19 HIV+ individuals responded to this epitope • Improved assay system (increase in culture time to 8 days and addition of IL-2 to cultures) gave increased detection of proliferative response				
p24 (51–66)	p24 (183–197)	DLNTMLNTYGGHQAAC	in vitro stimulation	human	Bedford1997
	• Epitope elicits a primary proliferative response in PBMC from uninfected donors				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (51–82)	Gag (183–214 LAI)	DLNTMLNTVGGHQAAMQML-KETINEEAAEWDR	Vaccine	human	Gahery-Segard2000
	Vaccine *Vector/Type:* lipopeptide • Anti-HIV lipopeptide vaccine consisting of six long peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial • A CD4+ T cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 2/10 reacted to this peptide • 9/12 tested mounted a CTL responses to at least one of the six peptides, each of the six peptides elicited a CTL response in at least one individual • None of the 12 tested had an IgG response to this peptide				
p24 (69–88)	Gag (p24) (201–220 IIIB)	LKETINEEAAEWDRVHPVHA	in vitro stimulation	human (DR)	Venturini2002
	• Epitope name: P21 • PBMC from a seronegative donor, the healthy brother of a pair of monozygotic twins discordant for HIV-1 infection, were used to generate HIV-1 Gag-specific CD4+ T-cell clones by in vitro immunization with HIV-1 overlapping 20mer peptides spanning p55. Six clones were generated by limiting dilution. All reacted with p24 except one which recognized a p24 peptide and a p6 peptide. All CD4+ T cell clones were HLA clas II DR restricted. • Clone 85 recognized this peptide using TCR Vbeta 8 and 18; the two TCR receptors indicates this limiting dilution represents a mixed population. This clone was only activated by peptide, not by processed protein from vaccinia virus Gag-infected B-LCL.				
p24 (71–86)	p24 (203–217)	ETINEEAAEWDRVHPC	in vitro stimulation	human	Bedford1997
	• Epitope elicits a primary proliferative response in PBMC from uninfected donors				
p24 (73–97)	p24 (205–229 PV22)	INEEAAEWDRVHPVHAGPI-APGQMR	HIV-1 infection	human (DRB1*03)	Lotti2002
	• 10/49 chronically HIV-1 infected patients had low p55-Gag-specific CD4+ T cell responses prior to therapy, and these responses remained unchanged 3 and 6 months after initiation of HAART. There was no difference in level of response in those with or without a detectable p55 response. • For one individual, patient F45 CDC stage A2, CD4+ p55 responding clones were generated. Her response was consistently strong and heterogeneous in terms of HLA restriction and Vbeta usage, and some clones had a Th1 cytokine secretion profile (high IFNgamma production) while some had a Th2 profile (high IL-4 and IL-5 production). 5/10 CD4+ clones could also induce cytotoxicity. • 4/10 clones from patient F45 had their epitopes mapped using overlapping peptides. Clone 12 recognized this peptide sequence restricted by DRB1*03 using TCR Vbeta 22. This clone had a SI of 12.4 to p55, 49.6 to peptide, secreted low levels of IFNgamma, indicative of a Th1 response. Clone 12 had cytotoxic activity, mediated through both a perforin and a Fas-based pathway.				
p24 (76–85)	p24 (208–217)	EAAEWDRVHP	HIV-1 infection	human	Adams1997
	• One of four immunogenic Gag peptides used in study of the proliferative response to p24 • T-cells from 11 of 24 HIV+ individuals responded to this epitope • Improved assay system (increase in culture time to 8 days and addition of IL-2 to cultures) gave increased detection of proliferative response				
p24 (76–90)	p24 (208–222 IIIB, B10)	EAAEWDRVHPVHAGP	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				
p24 (81–95)	p24 (215–229 SF2)	DRVHPVHAGPIAPGQ	Vaccine	macaque	Mills1990
	Vaccine *Vector/Type:* virus-like particle *Strain:* SF2 *HIV component:* p24 • Responses to 3 T-cell and multiple linear B-cell epitopes were found in vaccinated macaques				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (81–102)	p24 (213–234 SF2)	DRVHPVHAGPIAPGQMREP-RGS	HIV-1 infection	human	Rosenberg1997
	• While anti-HIV CD4 Th responses are characteristically undetectable in chronic infections, strong p24-specific proliferative responses were inversely correlated with low viral load in 10 chronically infected people • The dominant proliferative response in one of two long term survivors was to this peptide				
p24 (86–94)	p24 (NY5)	VHAGPIAPG	HIV-1 infection	human (DQ7)	Norris2001
	• Gag-specific CD4+ helper T-cell clones were derived from one long-term non-progressor (LTNP) (CTS-01), and three individuals given therapy during acute infection, two before (AC-01 and AC-36) and one after (AC-25) STI. Gag peptide recognition induced proliferation, IFNgamma production and perforin-mediated cytotoxicity in all CD4+ T-cell clones isolated. • 3/23 p24-derived peptides tested induced proliferative p24-specific T-helper cell responses in the LTNP CDT-01. The immunodominant response was to the peptide DRVHPVHAGPIAPGQMREPRGS (81-102), and 9/10 CD4+ T-cell clones reacted with it. One was characterized in detail and used a Bbeta4 TCR. • The minimum peptide recognized by the clones from CDT-01 was VHAGPIAPG and it was restricted by HLA-DQ7.				
p24 (87–101)	p24 (219–233 BRU)	HAGPIAPGQMREPRG	in vitro stimulation	murine (H-2^b)	Vaslin1994
	• Peptide G2: could prime for in vitro immunoproliferative responses and for subsequent IgG responses				
p24 (96–103)	p24 (228–235 LAI)	MREPRGSD	HIV-1 infection	human	Schrier1989
	• Stimulates T-cell proliferation in HIV-infected donors				
p24 (96–110)	p24 (228–242 IIIB, B10)	MREPRGSKIAGTTST	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				
p24 (99–118)	Gag (p24) (231–250 IIIB)	PRGSDIAGTTSTLQEQIGWM	in vitro stimulation	human (DR4)	Venturini2002
	• Epitope name: P24 • PBMC from a seronegative donor, the healthy brother of a pair of monozygotic twins discordant for HIV-1 infection, were used to generate HIV-1 Gag-specific CD4+ T-cell clones by in vitro immunization with HIV-1 overlapping 20mer peptides spanning p55. Six clones were generated by limiting dilution. All reacted with p24 except one which recognized a p24 peptide and a p6 peptide. All CD4+ T cell clones were HLA clas II DR restricted. • Clone 6 recognized three peptides including this one with a Th1 response using TCR Vbeta 6 (6s5A1N1). Sequencing TCR Vbeta regions of colonies from clone 6 suggested this was a clonal population. Assays using different peptide concentrations suggest that this peptide does not carry the main epitope of this clone.				
p24 (101–115)	p24 (235–249 SF2)	GSDIAGTTSTLQEQI	Vaccine	macaque	Mills1990
	Vaccine *Vector/Type:* virus-like particle *Strain:* SF2 *HIV component:* p24 • Responses to 3 T-cell and multiple linear B-cell epitopes were found in vaccinated macaques – epitope response defined by T-cell clone				
p24 (101–116)	p24	GSDIAGTTSTLQEQIC	in vitro stimulation	human	Bedford1997
	• Epitope elicits a primary proliferative response in PBMC from uninfected donors				
p24 (109–128)	Gag (p24) (241–260 IIIB)	STLQEQIGWMTNNPPIPVGE	in vitro stimulation	human	Venturini2002
	• Epitope name: P25 • PBMC from a seronegative donor, the healthy brother of a pair of monozygotic twins discordant for HIV-1 infection, were used to generate HIV-1 Gag-specific CD4+ T-cell clones by in vitro immunization with HIV-1 overlapping 20mer peptides spanning p55. Six clones were generated by limiting dilution. All reacted with p24 except one which recognized a p24 peptide and a p6 peptide. All CD4+ T cell clones were HLA clas II DR restricted.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Clone 50 recognized this peptide with a Th0 response (Th0 means that cytokines characteristic of both Th1 and Th2 responses were stimulated), using TCR Vbeta 17, and was a homogeneous T-cell population. This clone was only activated by peptide, not by processed protein from vaccinia virus Gag-infected B-LCL.				
p24 (111–132)	p24 (243–264 SF2)	LQEQIGWMTNNPPIPVGEI-YKR	HIV-1 infection	human	Rosenberg1997
	• Low viral load correlated with strong HIV-1-specific proliferative response • A proliferative response to this epitope was detected in two long term survivors				
p24 (119–133)	p24 (251–265)	TNNPPIPBGEIYKRW	HIV-1 infection	human (DRB1*1301)	Blankson2001b, Malhotra2001
	• The DRB1*13-DQB1*06 haplotype is associated with maintained viral suppression after HAART – 7/7 early-treated DRB1*13-DQB1*06 positive people, but only 3/14 (21%) of those who did not have DRB1*13-DQB1*06, maintained viral suppression for 18 months • PBMC from individuals with the haplotype DRB1*13-DQB1*06 displayed increased IFNγ secretion and stronger proliferative responses against p24 80 weeks post treatment • DRB1*13-DQB1*06 was also found to be enriched among long-term non-progressors (LTNPs) (it was in 9/18 versus, versus 21% of the general population) • This epitope was mapped with truncated peptides using the Elispot assay • Two distinct DRB1*13 epitopes were defined in the peptide region spanning 251 to 270, and this 20-mer bound with very high affinity to DRB1*1302 – DRB1*1301 and DRB1*1302 would be expected to have very similar binding properties				
p24 (121–136)	p24 (253–267)	NPPIPVGEIYKRWIIC	in vitro stimulation	human	Bedford1997
	• Epitope elicits a primary proliferative response in PBMC from uninfected donors				
p24 (121–140)	Gag (253–272 SF2)	NPPIPVGEIYKRWILGLNK	Vaccine	murine (H-2^d)	Mata1999
	Vaccine *Vector/Type:* Listeria moncytogenes *Strain:* SF2 *HIV component:* p24 • Listeria moncytogenes is an intracellular bacterium that lives in the cytoplasm and generates a cell-mediated immune response • Listeria moncytogenes vaccine expressing HIV-1 p24 protein (Lm-Gag) was used to stimulate gag specific CD4+ T cell proliferative responses in BALB/c(H-2d) and C57BL/6(H-2b) mice • Two of three reactive p24 peptides (out of 22 overlapping peptides that span p24) were recognized by both murine strains – this epitope is immunodominant in BALB/c mice and did not stimulate a C57BL/6 response • The proliferative response is due to CD4+, IFN-gamma producing cells, a Th1 response				
p24 (121–140)	p24 (253–272 HXB2)	NPPIPVGEIYKRWIILGLNK	Vaccine	murine (H-2^d)	Mata1999
	Vaccine *Vector/Type:* Listeria monocytogenes *Strain:* HXB2 *HIV component:* Gag • BALB/c and C57BL/6 mice were immunized with rec Listeria monocytogenes (Lm-Gag) expressing HIV-1 HXB2 Gag • L. monocytogenes is a gram-positive bacteria that enters the macrophage on phagocytosis and lives in the cytoplasm – secreted L. monocytogenes antigens are processed and presented by both class I and class II pathways • The class II T helper response was probed using 20 mer peptides that overlapped by 10, and the peptide MPPIPVGEIYKRWIILGLNK gave the immunodominant response for the H-2^d haplotype, but was not recognized in H-2^b mice				
p24 (121–152)	Gag (183–214 LAI)	NPPIPVGEIYKRWIILGLN-KIVRMYSPTSILD	Vaccine	human	Gahery-Segard2000
	Vaccine *Vector/Type:* lipopeptide • Anti-HIV lipopeptide vaccine consisting of six long peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• A CD4+ T cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 9/10 reacted to this peptide • 9/12 tested mounted a CTL responses to at least one of the six peptides, each of the six peptides elicited a CTL response in at least one individual – this peptide was particularly immunogenic, eliciting a CTL response in four vaccinees • All of the 12 tested had an IgG response to this peptide				
p24 (127–141)	Gag (294–308)	GEIYKRWIILGLNKI	HIV-1 infection	human (DR supermotif)	Wilson2001
	• Epitope name: Gag 294 • Eleven peptides were identified that had the HLA-DR supermotif, all were found to bind to MHC class II DR molecules and all elicted proliferative responses from multiple HIV-infected donors • This epitope binds ten HLA-DR alleles: DRB1*0101, DRB1*1501, DRB1*0405, DRB1*1101, DRB1*1302, DRB1*0701, DRB1*0802, DRB1*0901, DRB5*0101 and DRB4*0101 with an IC_{50} threshold below 1,000 nM • This epitope sequence is conserved in 95% of clade B isolates • 6/22 HIV infected individuals responded to this epitope (13/22 responded to some of the DR supermotif epitopes, the 9 non-responder peptides tended to also not have recall responses to rec HIV-1 whole proteins)				
p24 (128–137)	p24 (260–269)	EIYKRWIILG	HIV-1 infection	human (DRB1*1301, DRB1*1302)	Blankson2001b, Malhotra2001
	• The DRB1*13-DQB1*06 haplotype is associated with maintained viral suppression after HAART – 7/7 early-treated DRB1*13-DQB1*06 positive people, but only 3/14 (21%) of those who did not have DRB1*13-DQB1*06, maintained viral suppression for 18 months • PBMC from individuals with the haplotype DRB1*13-DQB1*06 displayed increased IFNγ secretion and stronger proliferative responses against p24 80 weeks post treatment • DRB1*13-DQB1*06 was also found to be enriched among long-term non-progressors (it was in 9/18 versus, versus 21% of the general population) • The truncated peptide that gave the optimal proliferative response for a Th1 phenotype clone was this nine-mer • This region, shared by 2 overlapping peptides, was the reactive region for clones from two DRB1*13 patients, one carried DRB1*1301 and one DRB1*1302 • Two distinct epitopes were defined in the peptide region spanning 251 to 270, and this 20-mer bound with very high affinity to DRB1*1302 – DRB1*1301 and DRB1*1302 would be expected to have very similar binding properties				
p24 (129–148)	Gag (p24) (261–280 IIIB)	IYKRWIILGLNKIVRMYSPT	in vitro stimulation	human	Venturini2002
	• Epitope name: P27 • PBMC from a seronegative donor, the healthy brother of a pair of monozygotic twins discordant for HIV-1 infection, were used to generate HIV-1 Gag-specific CD4+ T-cell clones by in vitro immunization with HIV-1 overlapping 20mer peptides spanning p55. Six clones were generated by limiting dilution. All reacted with p24 except one which recognized a p24 peptide and a p6 peptide. All CD4+ T cell clones were HLA clas II DR restricted. • Clone 74 recognized two peptides including this one with a Th1 response using TCR Vbeta 13 (13s1); it required 200 ng/ml (100 nM) and 1 μg/ml (0.5 μM) for stimulation by peptides 480-500 and 261-280, respectively. Sequencing TCR Vbeta regions of colonies from clone 74 suggested this was a clonal population.				
p24 (131–145)	p24 (265–279 SF2)	KRWIILGLNKIVRMY	Vaccine	macaque	Mills1990
	Vaccine *Vector/Type:* virus-like particle *Strain:* SF2 *HIV component:* p24 • Responses to 3 T-cell and multiple linear B-cell epitopes were found in vaccinated macaques – epitope response defined by T-cell clone				
p24 (131–145)	Gag (298–312)	KRWIILGLNKIVRMY	HIV-1 infection	human (DR supermotif)	Wilson2001
	• Epitope name: Gag 298				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Eleven peptides were identified that had the HLA-DR supermotif, all were found to bind to MHC class II DR molecules and all elicited proliferative responses from multiple HIV-infected donors • This epitope binds thirteen HLA-DR alleles: DRB4*0101, DRB5*0101, DRB1*0901, DRB1*0802, DRB1*0701, DRB1*1302, DRB1*1201, DRB1*1101, DRB1*0405, DRB1*0401, DRB*0301, DRB1*1501 and DRB1*0101, with an IC_{50} threshold below 1,000 nM • This epitope sequence is conserved in 94% of clade B isolate • 8/22 HIV infected individuals responded to this epitope (13/22 responded to some of the DR supermotif epitopes, the 9 non-responder peptides tended to also not have recall responses to rec HIV-1 whole proteins)			
p24 (131–152)	p24 (263–284 SF2)	KRWIILGLNKIVRMYSPTS-ILD	HIV-1 infection	human	Rosenberg1997
	• Low viral load correlated with strong HIV-1-specific proliferative response • A proliferative response to this epitope was detected in two long term survivors				
p24 (135–154)	p24 (267–286)	ILGLNKIVRMYSPTSILDIR	HIV-1 infection	human	Adams1997
	• One of four immunogenic Gag peptides used in study of the proliferative response to p24 • 8 of 24 HIV+ individuals responded to this epitope • Improved assay system (increase in culture time to 8 days and addition of IL-2 to cultures) gave increased detection of proliferative response				
p24 (139–157)	Gag (p24) (271–290 IIIB)	NKIVRMYSPTSILDIRQGP	in vitro stimulation	human (DR4)	Venturini2002
	• Epitope name: P28 • PBMC from a seronegative donor, the healthy brother of a pair of monozygotic twins discordant for HIV-1 infection, were used to generate HIV-1 Gag-specific CD4+ T-cell clones by in vitro immunization with HIV-1 overlapping 20mer peptides spanning p55. Six clones were generated by limiting dilution. All reacted with p24 except one which recognized a p24 peptide and a p6 peptide. All CD4+ T cell clones were HLA clas II DR restricted. • Clone 6 recognized three peptides including this one with a Th1 response using TCR Vbeta 6 (6s5A1N1). Sequencing TCR Vbeta regions of colonies from clone 6 suggested this was a clonal population. Assays using different peptide concentrations suggest that this peptide, 271-290, contains the main epitope of this clone. Upon activation, clone 6 was observed to induce a cytopathic effect in the adherent layer of fibroblasts expressing HLA DR4W14 and -W15. Clone 6 was activated in response to vaccinia virus Gag-infected B-LCL, so could recognize naturally processed epitopes. • Clone 37 recognized this peptide sequence with a Th2 response using TCR Vbeta 3, and was a homogeneous T-cell population. This clone was only activated by peptide, not by processed protein from vaccinia virus Gag-infected B-LCL. • Clone 97 recognized this peptide sequence with a using TCR Vbeta 9 and 14; the two TCR receptors used indicates this limiting dilution represents a mixed population. This clone was only activated by peptide, not by processed protein from vaccinia virus Gag-infected B-LCL.			
p24 (141–156)	p24 (273–287)	IVRMYSPTSILDIRQC	in vitro stimulation	human	Bedford1997
	• Epitope elicits a primary proliferative response in PBMC from uninfected donors • Matches 3/3 anchor residues for HLA DR: **I**VRMY**S**PT**S**				
p24 (146–160)	p24 (278–292 IIIB, B10)	SPTSILDIRQGPKEP	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				
p24 (149–168)	Gag (p24) (281–300 IIIB)	SILDIRQGPKEPFRDYVDRF	in vitro stimulation	human (DR4)	Venturini2002
	• Epitope name: P29				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• PBMC from a seronegative donor, the healthy brother of a pair of monozygotic twins discordant for HIV-1 infection, were used to generate HIV-1 Gag-specific CD4+ T-cell clones by in vitro immunization with HIV-1 overlapping 20mer peptides spanning p55. Six clones were generated by limiting dilution. All reacted with p24 except one which recognized a p24 peptide and a p6 peptide. All CD4+ T cell clones were HLA clas II DR restricted. • Clone 6 recognized three peptides including this one with a Th1 response using TCR Vbeta 6 (6s5A1N1). Sequencing TCR Vbeta regions of colonies from clone 6 suggested this was a clonal population. Assays using different peptide concentrations suggest that this peptide does not carry the main epitope of this clone.				
p24 (150–169)	p24 (282–301)	ILDIRQGPKEPFRDYVDRFY	HIV-1 infection	human	Schrier1989
	• Stimulates T-cell proliferation in HIV-infected donors				
p24 (151–166)	p24 (283–297)	LDIRQGPKEPFRDYVC	in vitro stimulation	human	Bedford1997
	• Epitope elicits a primary proliferative response in PBMC from uninfected donors				
p24 (155–177)	p24 (287–309)	QGPKEPFRDYVDRFYKTLR-AEQA	Vaccine	murine	Nakamura1997
	Vaccine *Vector/Type:* peptide • Mice immunized with this peptide generated proliferative responses, CTLs and antibodies • This immunogenic domain is from a highly conserved region of p24				
p24 (156–170)	p24 (288–302 IIIB, B10)	GPKEPFRDYVDRFYK	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				
p24 (156–174)	p24 (287–306)	QPKEPFRDYVDRFYKTLRA	HIV-1 infection	human	Adams1997
	• One of four immunogenic Gag peptides used in study of the proliferative response to p24 • T-cells from 5 of 21 HIV+ individuals responded to this epitope • Improved assay system (increase in culture time to 8 days and addition of IL-2 to cultures) gave increased detection of proliferative response				
p24 (161–180)	Gag (293–312 SF2)	FRDYVDRFYKTLRAEQASQD	Vaccine	murine (H-2^d, H-2^b)	Mata1999
	Vaccine *Vector/Type:* Listeria moncytogenes *Strain:* SF2 *HIV component:* p24 • Listeria moncytogenes is an intracellular bacterium that lives in the cytoplasm and generates a cell-mediated immune response • Listeria moncytogenes vaccine expressing HIV-1 p24 protein (Lm-Gag) was used to stimulate gag specific CD4+ T cell proliferative responses in BALB/c(H-2d) and C57BL/6(H-2b) mice • Two of three reactive p24 peptides (out of 22 overlapping peptides that span p24) were recognized by both murine strains – this peptide stimulated a response in both BALB/c and C57BL/6 mice • The proliferative response is due to CD4+, IFN-gamma producing cells, a Th1 response				
p24 (161–180)	p24 (293–312 HXB2)	FRDYVDRFYKTLRAEQASQD	Vaccine	murine (H-2^d, H-2^b)	Mata1999
	Vaccine *Vector/Type:* Listeria monocytogenes *Strain:* HXB2 *HIV component:* Gag • BALB/c and C57BL/6 mice were immunized with rec Listeria monocytogenes (Lm-Gag) expressing HIV-1 HXB2 Gag • L. monocytogenes is a gram-positive bacteria that enters the macrophage on phagocytosis and lives in the cytoplasm – secreted L. monocytogenes antigens are processed and presented by both class I and class II pathways • The class II T helper response was probed using 20 mer peptides that overlapped by 10, and the peptides VHQAISPRTLNAWVKVVEEK and FRDYVDRFYKTLRAEQASQD were recognized in H-2^b and H-2^d mice				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (163–177)	p24 (295–309)	DYVDRFYKTLRAEQA	HIV-1 infection	human (DRB1*1302)	Blankson2001b, Malhotra2001
	• The DRB1*13-DQB1*06 haplotype is associated with maintained viral suppression after HAART – 7/7 early-treated DRB1*13-DQB1*06 positive people, but only 3/14 (21%) of those who did not have DRB1*13-DQB1*06, maintained viral suppression for 18 months • PBMC from individuals with the haplotype DRB1*13-DQB1*06 displayed increased IFNγ secretion and stronger proliferative responses against p24 80 weeks post treatment • DRB1*13-DQB1*06 was also found to be enriched among long-term non-progressors (it was in 9/18 versus, versus 21% of the general population) • This epitope was mapped with truncated peptides using the Elispot assay, and is highly conserved				
p24 (175–199)	p17 (307–331 PV22)	EQASQEVKNWMTETLLVQN-ANPDCK	HIV-1 infection	human (DRB1*03)	Lotti2002
	• 10/49 chronically HIV-1 infected patients had low p55-Gag-specific CD4+ T cell responses prior to therapy, and these responses remained unchanged 3 and 6 months after initiation of HAART. There was no difference in level of response in those with or without a detectable p55 response. • For one individual, patient F45 CDC stage A2, CD4+ p55 responding clones were generated. Her response was consistently strong and heterogeneous in terms of HLA restriction and Vbeta usage, and some clones had a Th1 cytokine secretion profile (high IFNgamma production) while some had a Th2 profile (high IL-4 and IL-5 production). 5/10 CD4+ clones could also induce cytotoxicity. • 4/10 clones from patient F45 had their epitopes mapped using overlapping peptides. Clone 26 recognized this peptide sequence restricted by DRB1*03. This clone had a SI of 4.1to p55, 5.3 to peptide, secreted high levels of IFNgamma, indicative of a Th1 response, but also IL-4 and IL-5. Clone 26 had no cytotoxic activity.				
p24 (181–196)	p24 (313–327)	VKNWMTETLLVQNANC	in vitro stimulation	human	Bedford1997
	• Epitope elicits a primary proliferative response in PBMC from uninfected donors • Matches 3/3 anchor residues for HLA DR: **V**KNWM**T**ET**L**				

III-B-3 p2p7p1p6 Helper T-Cell Epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p2p7p1p6 (30–44)	p15 (393–407 IIIB, B10)	FNCGKEGHTARNCRA	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				
p2p7p1p6 (55–69)	p15 (418–432 IIIB, B10)	KEGHQMKDCTERQAN	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				
p2p7p1p6 (60–74)	p15 (423–437 IIIB, B10)	MKDCTERQANFLGKI	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				
p2p7p1p6 (76–83)	p24 (439–446 LAI)	PSYKGRPG	HIV-1 infection	human	Schrier1989
	• Stimulates T-cell proliferation in HIV-infected donors • Schrier lists this peptide as p24(439-446), but because of the numbering used for Gag epitopes, we placed it in p2p7p1p6				
p2p7p1p6 (83–97)	p15 (446–460 BRU)	GNFLQSRPEPTAPPA	in vitro stimulation	murine (H-2^b)	Vaslin1994
	• Peptide G4: could prime for in vitro immunoproliferative responses and for subsequent IgG responses				
p2p7p1p6 (98–112)	p15 (473–487 IIIB, B10)	ESFRSGVETTTPPQK	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• Peptides were identified that commonly evoke T-cell responses – 50% of 90 HIV+ people had a T-cell response to this peptide				
p2p7p1p6 (103–110)	p24 (466–473 LAI)	REETTTPS	HIV-1 infection	human	Schrier1989
	• Stimulates T-cell proliferation in HIV-infected donors • Schrier lists this peptide as p24(466-473), but it is in p2p7p1p6.				
p2p7p1p6 (117–137)	Gag (p6) (480–500 IIIB)	DKELYPLTSLRSLFGNDPS-SQ	in vitro stimulation	human	Venturini2002
	• PBMC from a seronegative donor, the healthy brother of a pair of monozygotic twins discordant for HIV-1 infection, were used to generate HIV-1 Gag-specific CD4+ T-cell clones by in vitro immunization with HIV-1 overlapping 20mer peptides spanning p55. Six clones were generated by limiting dilution. All reacted with p24 except one which recognized a p24 peptide and a p6 peptide. All CD4+ T cell clones were HLA class II DR restricted. • Clone 74 recognized two peptides, including this one, with a Th1 response using TCR Vβ 13 (13s1); it required 200 ng/ml (100 nM) and 1 μg/ml (0.5 μM) for stimulation by peptides 480-500 and 261-280, respectively. Sequencing TCR Vbeta regions of colonies from clone 74 suggested this was a clonal population. Clone 74 was activated in response to vaccinia virus Gag-infected B-LCL, so could recognize naturally processed epitopes.				

III-B-4 Gag Helper T-Cell Epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Gag	p24		HIV-1 infection, Vaccine	human	Kelleher1998b
	Vaccine *Vector/Type:* virus-like particle *HIV component:* p24, p17				
	• Immunization of HIV+ people with a p24-VLP virus-like particle did not significantly impact CD4+ lymphocyte count, viral load, or p24 antibody titre				
	• Immunization with p24-VLP showed a modest, short-lived increased proliferative response to p24				
Gag	p24		HIV-1 infection, Vaccine	human	Maino2000
	Vaccine *Vector/Type:* protein, gp120 depleted virus HZ321 (REMUNE(TM)) *Strain:* Z321 *HIV component:* p24, gp120 depleted virus				
	• 18 HIV-1-seropositive patients with a low frequency or no detectable CD4+ T cell response to HIV-1 antigen received an HIV-1 immunogen consisting of 10 units of native p24 and 100 ug of HZ321, a gp120 depleted antigen				
	• Using flow-cytometric methods, HIV-1 specific CD4+ T cells were shown to increase in response to immunization – in many patients significant enhancement was observed after a single immunization				
	• The frequency of CD4+ T cells expressing cytokines in response to antigen by FACS was correlated with a lymphoproliferation assay				
Gag	p24		HIV-1 infection	human	Ruiz2000
	• Structured treatment interruption in chronically infected patients allowed recovery of p24 Th proliferative responses after HAART therapy discontinuation in 2/12 patients				
	• The Th response to p24 was identified during peak viremia in one patient, while in the second it was noted when viremia was controlled after restarting antiviral therapy				
Gag	p24		HIV-1 infection	human	Lori1999
	• Ten patients with acute, pre-seroconversion HIV-1 infections were treated with didanosine, indinavir and hydroxyurea – this treatment is associated with normalization of immune parameters				
	• A vigorous HIV-specific Th response (stimulation index greater than 8) was observed in 7/8 patients treated before complete WB seroconversion, but in only 1/5 controls treated after seroconversion				
	• Vigorous Th responses were detected as early as 34 days after treatment begin				
	• Patients treated prior to seroconversion had no loss of naive CD4 T lymphocytes, recovery of up to 35% of the naive CD8 cells in several weeks, and a reduced latent viral reservoir				
Gag	p24		HIV-1 infection	human	Haslett2000
	• 11/22 adult patients on HAART showed strong CD4+ T-cell IFN-gamma producing Th1 responses to HIV p24				
	• The magnitude of the Th1 response correlated with previous interruptions in HAART, suggesting the interruptions primed or boosted the response				
	• In contrast, the magnitude of the CD8+ CTL response did not correlate with interruptions in therapy, although a greater breadth in response was associated with interruptions in HAART				
Gag	p24		HIV-1 infection, Vaccine	human	Klein1997
	Vaccine *Vector/Type:* virus-like particle *HIV component:* p24, p17				
	• Immunization of HIV+ people with a HIV-1 p17/p24 Ty virus-like particle (p24-VLP) resulted in a marginal, short-lived increased proliferative response to p24 and p17 and a transient elevation in viral load				
	• Two of four subjects that received 500 or 1000 ug of p24-VLP had an increase in gag-specific CTL				
Gag	p24		Vaccine	human	Moss1998
	Vaccine *Vector/Type:* gp120 depleted virus HZ321 (REMUNE(TM)) *Strain:* Z321 *HIV component:* gp120 depleted virus				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Immunization with gp120 depleted HZ321 virus (REMUNE^{TM}) triggered an increase in lymphocyte proliferative response to native p24, a clade B virus and clade E viral antigens – Z321 is clade A in env and clade G in gag. [Moss1998]				
Gag	p24		HIV-1 infection	human	Rosenberg1999
	• This paper reviews the role of T-cells in viral control and HIV disease outcome • Strong anti-p24 lymphoproliferative responses were found in seven persons who were treated with potent anti-viral therapy during acute HIV-1 infection syndrome • This suggests that Th cells are part of the normal response to HIV-1 infection, but their numbers are rapidly diminished by either being infected during the peak viremia or by activation-induced cell death – if peak viremia can be controlled, a robust anti-p24 Th response can be maintained				
Gag	p24		HIV-1 infection	human	Rosenberg1998
	• Strong Th responses have been found in rare individuals who effectively maintain low viral loads • If aggressive anti-retroviral therapy is given prior to sero-conversion, strong helper responses can be maintained.				
Gag	p17		Vaccine	murine	Birk1998a
	Vaccine *Vector/Type:* recombinant protein *HIV component:* p17 • Different p17 genes derived from the same quasispecies and expressed and purified in E. coli primed different Th 1 and Th 2 subsets in mice, depending on their H-2 type.				
Gag	Gag		HIV-1 infection	human	Schiller2000
	• Study of parameters that might influence the performance or reproducibility of clinical Th proliferative assays • HIV-1 replication in vitro is unlikely to influence the assay • Gag proteins including p17 and possibly p7 as well as p24 perform better than p24 alone • Frozen samples can be used in T-proliferative assays, but with lower radiolabled thymidine incorporation				
Gag	Gag		HIV-1 infection	human	Pitcher1999
	• In contrast to earlier studies suggesting that HIV-1 specific Th responses were eliminated in the early stages of infection in most HIV+ individuals, this paper shows using flow cytometric detection of antigen-induced cytokines that Th-1 CD4+ memory gag-specific Th cells are detectable in most HIV+ subjects • Effective anti-viral therapy reduces the frequency of these cells, presumably due to reduced antigenic stimulus				
Gag	Gag		HIV-1 infection	human	Plana1998
	• Patients from later stages of infection given HAART do not show restoration of HIV-1 specific Th proliferative responses				
Gag	Gag		HIV-1 infection	human	Kelleher1998a
	• Env and gag Th epitopes were pooled and used to test Th proliferative responses after IL2 therapy – while IL2 therapy causes an increase in CD4+ lymphocyte count, it does not increase HIV-1 specific proliferative responses				
Gag	Gag (LAI)		Vaccine	Macaca nemestrina	Kent1998
	Vaccine *Vector/Type:* DNA prime with vaccinia boost *Strain:* LAI *HIV component:* ENV, GAG • Priming with an HIV-DNA vaccine and boosting with a vaccinia construct induced greater levels of HIV T-cell immunity than either vaccine alone • The proliferative response to Env and Gag after the DNA vaccination had a mean SI of 1.5-4, but after boosting with rHIV-fowlpox virus, there was a 6-17 fold increase in the mean SI for HIV Gag and Env – The Th response happened despite a fall in Ab titers, suggesting that the Th response was primarily Th1, not Th2. The CTL response was also enhanced				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Gag			Vaccine	Rhesus macaque	Heeney1999
	Vaccine *Vector/Type:* DNA, protein, virus-like particle, ISCOM • Ten different vaccine strategies were evaluated for their ability to protect from infection in a rhesus macaque model using a non-pathogenic SHIV challenge • Protection correlated with the magnitude of NAb responses, beta-chemokines, and a balanced Th response • DNA, protein+adjuvant, VLP and ISCOM vaccines were tested • HIV-1/ISCOMS gave the highest NAb titers, Th1 and Th2 responses, was the only vaccine formulation tested with a detectable CTL response, and gave enhanced beta-chemokine production				
Gag	Gag/Pol (MN)		Vaccine	chimpanzee	Kim1998
	Vaccine *Vector/Type:* DNA *Strain:* MN *HIV component:* GAG, POL, ENV *Adjuvant:* CD80 and CD86 expression vectors • Co-stimulatory molecules co-expressed with an HIV-1 immunogen in a DNA vaccine used to enhance the immune response – co-expression of CD86, but not CD80, dramatically increased both HIV Env and Gag/Pol specific CTL and Th proliferative responses				
Gag	Gag/Pol (LAI, MN)		Vaccine	human	Salmon-Ceron1999
	Vaccine *Vector/Type:* canarypox *Strain:* MN, LAI *HIV component:* gp120, gp41, Gag, Protease • A live attenuated canarypox vector expressing MN gp120 and LAI gp41/gag/protease could induce CTL and a lymphoproliferative response in healthy uninfected volunteers				
Gag	p55 (IIIB)		HIV-1 infection	human	Zhang2001b
	• T-helper cell proliferative responses to HIV p24, p55 and gp120 were tested in 27 patients with HIV infection – vigorous responses directed at Gag were detected in ten patients, but an Env specific response was detected in only one patient • Untreated patients showed a negative correlation between plasma viral load and HIV p24-specific T-cell responses, and the responses could be detected after extended HAART therapy with viremia below the detection limit				
Gag	p24		HIV-1 infection	human	Carcelain2001
	• Repeated structured HAART therapy interruptions (STI) in 3 chronically HIV infected patients induced rapid but transient (< 3 weeks) HIV-1 specific CD4+ Th1 responses concurrently with viral rebound, as measured by proliferation assays and by IFNγ production by CD8-depleted PBMC • Kinetics suggest that viral replication leads to rapid destruction of the HIV-specific Th1 cell response • HIV-specific CD8+ T-cell responses were delayed relative to the Th1 responses and were not sustained				
Gag	Gag		HIV-1 infection	human	Blankson2001a
	• 5/10 chronically HIV infected patients with low CD4+ counts who received HAART therapy and experienced immune reconstitution displayed p24, p17 and p66 T-helper CD4 proliferative responses, in contrast to 0/8 chronically HIV infected patients with high CD4+ counts at the initiation of antiretroviral treatment • This surprising result could be due to the low CD4 nadir patients being more likely to have thymic regeneration or a peripheral expansion of T cells				
Gag	p24		HIV-1 infection	human	Angel2001
	• Prolonged viral suppression resulting from potent anti-retroviral therapy allowed a T helper response to Gag p24 and PHA to develop in many HIV+ patients • At baseline, 2/41 (4.9%) subjects had a proliferative response to Gag p24, and 7/41 (17.1%) had a response to PHA, but by week 72 of therapy, 53% had a detectable response to p24 and 94% to PHA				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Gag	p24		HIV-1 infection	human	Blazevic2000
• Prolonged viral suppression resulting from potent anti-retroviral therapy did not allow an HIV T helper response to p24 or gp160, but Th proliferative responses to influenza, alloantigen, and PHA did develop in many HIV+ patients, and asymptomatic patients had stronger and more frequent Th response recovery than AIDS patients					
Gag	Gag (SF2)		HIV-1 infection	human	Altfeld2001b
• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the CTL response was determined using Elispot by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Individuals who were given HAART during acute or early in infection had significantly stronger proliferative responses than individuals who were chronically infected					
Gag	p24		HIV-1 infection	human	Oxenius2000
• Patients who started therapy at acute HIV infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV-specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV-specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable • In 3/4 responders tested p24 gave the strongest T helper response					
Gag	p24		Vaccine	rat	Moss2001
Vaccine *Vector/Type:* gp120 depleted whole killed virus *Strain:* HZ321 (subtype A env, subtype G gag) *HIV component:* whole virus *Adjuvant:* CpG, Freund's adjuvant • Lewis rats simultaneously immunized with HIV-1 antigen and with immunostimulatory sequences CpG had increased Th proliferative responses, but when CpG was given as a prime prior to the injection of HIV-1 antigen it was not as effective					
Gag	p24		Vaccine	rat	Moss2000
Vaccine *Vector/Type:* gp120 depleted whole killed virus *Strain:* HZ321 (subtype A env, subtype G gag) *HIV component:* whole virus *Adjuvant:* CpG, Freund's adjuvant • Lewis rats co-immunized with HIV-1 antigen in Freund's and with immunostimulatory sequences CpG stimulated increased IFNγ expressing CD4+ and CD8+ T cells and anti-p24 antibodies relative to antigen in Freund's without CpG					
Gag	p24		HIV-1 infection	human	Kalams1999a
• The strength of p24 specific Gag proliferative responses (SIs) were inversely correlated with viral load in 21 ARV naive patients. The responses were Th1, IFNγ producing. Proliferative responses against gp160 were rarely observed (only 4 cases). • Gag specific CTL levels were correlated with Gag proliferative responses but were not correlated with viral load. 8 subjects lacked p24 specific Gag proliferative responses, and 4/8 had no CTLp to any HIV-1 antigen tested.					
Gag	p24		HIV-1 infection	human	Kalams1998
• This paper reviews the role of specific T cell help in many viral infections, and covers the interplay between Th, CTL and survival, and discusses briefly advantages of HAART during acute HIV infection to prevent the early decimation of the Th response in HIV infections.					
Gag	p24		HIV-1 infection	human	Wilson2000b
• Dysfunction of HIV-1 specific proliferative responses, but not responses to other antigens, is evident in HIV-1 progressive disease.					

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Vigorous HIV-1 specific responses to p24, Nef and gp120 with SI between 8-99 were seen in 6/7 long term non-progressors (LTNP), the seventh had a borderline responses. IL-2 production was seen in all cases, and IL-4 production was also evident many responses. • None of the progressors (0/5) had HIV-1 specific proliferative responses, or IL-2 or IL-4 induction. • Non-HIV antigens (cytomegalovirus, PPD, Staphylococcus enterotoxin B, tetanus toxoid) gave similar responses in HIV-1+ LTNP, progressors, and HIV-1 controls.				
Gag	p24		HIV-1 infection	human	Alatrakchi2002
	• LTNP co-infected with HCV and HIV showed higher frequencies of Th1 response to both HIV-1 p24 and HCV antigens. • HIV-1 CD4 Th1 responses in untreated LTNP were inversely correlated with viral load.				
Gag	p24		HIV-1 infection	human	Lange2002
	• Cross-sectional study compares CD4 T-cell count and age matched untreated HIV-1+ patients (N = 14) with patients undergoing HAART therapy (N = 14). • The fractions of naive and memory T-cells were comparable for both groups, as were proliferative responses to non-HIV antigens. Lymphocyte proliferation responses to HIV-1 p24 were of greater magnitude in the group treated with HAART (5/10 had SI >10, versus 1/12 in the untreated group), suggesting that ongoing viral replication impairs the anti-Gag response, and the response can be improved and restored through HAART. • DTH responses to recall antigens were tested, and responses to C. albicans and Trichophyton were comparable in both treated and untreated patients, although patients on therapy had higher responses to mumps.				
Gag	p24		HIV-1 infection	human	Fidler2002
	• 37/45 patients with primary HIV infection underwent a short course of antiretroviral therapy (SCART). 29/37 patients received triple ART therapy and eight patients received four ART drugs. Initiation of SCART was effective in controlling HIV replication by ten weeks in all patients and preserving CD4+ T cell responses for up to 64 weeks after therapy. • No induction of drug escape mutations was observed, although two individuals had escape mutations in their infecting virus at baseline. • 34 UK infected patients were clade B infected. 11/45 subjects had non-UK acquired HIV infection, 2 were clade A, 1 was A/E, 1 was C, 1 was "untypable", the rest were B. • Recombinant HIV-1 derived gp120, p24, p66 and overlapping peptide pools spanning Tat and Nef were employed to measure CD4 T-cell frequencies in ELISPOT assays. The strongest preservation of T helper responses 12 weeks off SCART was seen for p24-specific CD4+ T-cell responses. • 6/8 of the untreated individuals were tested for CD4+ T-cell responses. 1 had no detectable response. 1 had detectable responses to all HIV-1 proteins tested at baseline, but this narrowed to p24 and gp120, then became undetectable by 52 weeks. 3 had detectable and persistent responses, but only to p24. • Post-therapy, the average spot forming cells for all proteins tested in 17/37 with 24 weeks of follow up had not declined, although the plasma viral RNA was increasing. SFU using p24 were measurable following SCART and preserved at levels comparable to baseline.				
Gag			Vaccine	human	Klein1997, Lindenburg2002
	Vaccine *Vector/Type:* virus-like particle *Strain:* IIIB *HIV component:* p17, p24 *Adjuvant:* aluminum hydroxide • HIV-1 p17/p24:Ty virus-like particles therapeutic vaccination of 56 HIV-1 infected patients had no effect on disease progression, AIDS and CD4+ T-cell decline in a longitudinal study, despite some evidence suggesting it can enhance Th anti-Gag proliferative responses in HIV+ individuals [Klein1997]				
Gag	p24 (NY5)		HIV-1 infection	human	Norris2001
	• Gag-specific CD4+ helper T-cell clones were derived from one long-term non-progressor (LTNP) (CTS-01), and three individuals given therapy during acute infection, two before (AC-01 and AC-36) and one after (AC-25) STI. • The immunodominant response in LTNP CTS-01 was to peptide 9, and 9/10 clones derived from this patient reacted with it. Three, two, and one clones were obtained from the three patients given therapy. These six clones all reacted with different p24 peptides, and all had peptide induced proliferative responses, IFNgamma production, and cytotoxic responses. The implications of cytoxic responses in CD4+ T-helper cells are discussed.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Gag	p24		HIV-1 infection	human	Palmer2002
• CD4+ T cell proliferative responses from 33 HIV-1 infected patients with HAART suppression were compared to 19 patients with active viral replication (HAART failures and HAART naive). Patients with HAART suppression showed stronger p24- and p66-specific proliferative responses compared to patient groups with active HIV-1 replication, suggesting active viral replication in vivo specifically reduces proliferation responses. • No differences in the frequency of HIV-specific CD4+ T-cells that were positive for cytokine secretion in a flow cytometry assay were found in the HAART suppressed group versus the group with active viral replication.					
Gag	p24 (SF2)		HIV-1 infection	human	Imami2002b
• 70 patients with chronic disease progression, 10 clinical non-progressors, and 3 immunologically discordant progressors (individuals who controlled viremia but had progressive CD4+ T-cell decline) were analyzed for their T-helper cell responses to p24 and cytokine profile. • SF2 p24 20mer peptides overlapping by 10 were used to assess the response in the different groups. At least 1/10 and up to 7/10 nonprogressors had a proliferative response with every one of the 22 p24 overlapping peptides. All peptides produced an IL-2 (Th1) response in at least one of the 10 nonprogressors. IL-4 (Th2) responses were strong, but somewhat less comprehensive as 6/22 peptides elicited no IL-4 production, and fewer IL-4 responses were see per peptide. In contrast, only 1/10 progressors had a clear proliferative and IL-2 response to 2/22 peptides, and neither one made an IL-4 response. • The results taken together suggest that a balanced Th1/Th2 response to HIV is important for viral control in long-term non-progression. • One immunologically discordant progressor became symptomatic while on the study. He showed a rapid decline in proliferative activity at that point, and a shift from a Th1 to a Th2 IL-4 producing response.					
Gag	(BRU)		Vaccine	murine	Haas1991
Vaccine *Vector/Type:* inactivated virus *Strain:* BRU *HIV component:* whole virus *Adjuvant:* Complete Freund's adjuvant (CFA) • Of 5 mouse inbred lines tested: DBA/2 (H-2d, Ad, Ed), B10.A(4R) (H-2h4, Ak) and B10.A(5R) (H-2i5) showed particularly good CD4+ T cell proliferative responses to HIV proteins (gp160, gp120, p17, p24, Nef and RT), after vaccination with inactivated virus. • B10.BR (H-2k, Ak, Ek) and C57BL/6 (H-2b and Ab) had weaker responses.					
Gag	p24 (IIIB)		in vitro stimulation	human (A*0201)	Engelmayer2001
• Recombinant canarypox virus vector containing HIV-1 sequences, upon infection of mature dendritic cells, can trigger specific lysis in vitro by T-cells from HIV-1 infected individuals at levels comparable to the response seen to HIV carried in vaccinia vectors • Recombinant canarypox virus vector containing HIV-1 sequences can also stimulate HIV-specific IFNγ CD4+ helper T cell responses to Gag from bulk or purified CD4+ T cells					
Gag	p55		HIV-1 infection	human (DRB1*13, DRB1*03)	Lotti2002
• 10/49 chronically HIV-1 infected patients had low p55-Gag-specific CD4+ T cell responses prior to therapy, and these responses remained unchanged 3 and 6 months after initiation of HAART. There was no difference in level of response in those with or without a detectable p55 response. • For one individual, patient F45 CDC stage A2, CD4+ p55 responding clones were generated. Her response was consistently strong and heterogeneous in terms of HLA restriction and Vbeta usage. Two clones were DRB1*13 restricted and used TCR Vbeta 17+19 or 5.1. Three clones were DRB1*03 restricted and used TCR Vbeta 22. Some clones had a Th1 cytokine secretion profile (high IFNgamma production) while some had a Th2 profile (high IL-4 and IL-5 production).					
Gag	p24		Vaccine	murine (H-2^d)	Qiu2000
Vaccine *Vector/Type:* DNA *HIV component:* GAG • Mice were injected with plasmid DNA at 0, 2 and 4 weeks and lymphocyte proliferation was measured after 6 weeks with recombinant p24 protein • Secreted HIV-1 Gag expression vectors generated a stronger response than standard Gag or cytoplasmic Gag expression vectors • IFN-gamma levels were increased compared to an undetectable IL-4 response					

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• CTL levels were also increased in secreted Gag expression vaccination studies				
Gag	Gag		Vaccine	murine (H-2^d)	Billaut-Mulot2001
	Vaccine *Vector/Type:* DNA with DNA boost, DNA with recombinant protein boost *Strain:* LAI *HIV component:* Gag, Tat, Nef *Adjuvant:* IL18				
	• DNA vaccinated BALB/c mice primed and boosted with a multiepitopic vaccine with IL18 showed lymphoproliferative responses 7 weeks post immunization				
	• Strong but non-lasting HIV-specific CTL responses were detected by a Cr-release assay and DNA prime + DNA boost was more effective than DNA prime + protein boost				
	• Immunization with either the multiepitopic DNA or with the mixed DNA vaccine resulted in Th1 cytokines production (IL-2 and IFNγ) in spleen cell cultures stimulated by Tat and Gag, while Th2 cytokines IL-4 and IL-10 production was not detectable				
	• Co-administration of IL18 increased T-cell responses but decreased anti-HIV antibody levels				
Gag	p24		Vaccine	murine (H-2^d)	Halim2000
	Vaccine *Vector/Type:* coxsackievirus *HIV component:* partial p24, polyepitope				
	• An avirulent rec coxsackievirus (CB4-P) construct was generated that can express p24 Gag sequences – CB4-P is attenuated even in immunodeficient mice and T help responses can be elicited from peptides embedded in a surface loop of the VP1 capsid				
	• This paper describes the vaccine strategy and generation of constructs, and employs amino-terminal fusion of Gag sequences to the viral polyprotein with subsequent cleavage to elicit CTL responses via MHC class I presentation in BALB/c mice				
Gag	gp120 (V3) and p24 (IIIB, MN, BH10)		Vaccine	murine (H-2^d)	Buonaguro2002
	Vaccine *Vector/Type:* virus-like particle *Strain:* gp120 A clade UG5.94UG018, HIV-1 IIIB *HIV component:* gp120 and Pr55gag				
	• BALB/c mice were given intraperitoneal immunization in the absence of adjuvants with virus-like particles (VLPs) expressing recombinant subtype A gp120 and Pr55gag				
	• High dose-independent humoral responses were elicited against both gp120 and p24 peptides, and CTL responses were observed against target cells carrying vaccinia expressed gp120 and Gag.				
Gag	Gag (HXB2)		Vaccine	murine (H-2^d, H-2^b)	Mata2001
	Vaccine *Vector/Type:* Listeria monocytogenes *Strain:* HXB2 *HIV component:* Gag				
	• BALB/c and C57BL/6 mice were immunized with rec Listeria monocytogenes (Lm-Gag) expressing HIV-1 HXB2 Gag and mice were challenged with vaccinia expressing Gag				
	• L. monocytogenes is a gram-positive bacteria that enters the macrophage on phagocytosis and lives in the cytoplasm – secreted L. monocytogenes antigens are processed and presented by both class I and class II pathways				
	• CD4+ Th1 T-cells mediated the Gag specific immunological protection in mice immunized with Lm-Gag and challenged with vaccinia-Gag				
	• Gag-specific CTL may enhance viral clearance via IFNγ secretion, but are not essential for immunity				
Gag	Gag		Vaccine	murine (H-2^d, H-2^b)	Mata2000
	Vaccine *Vector/Type:* Listeria monocytogenes *HIV component:* Gag				
	• BALB/c and C57BL/6 mice were immunized with rec Listeria monocytogenes (Lm-Gag) expressing HIV-1 HXB2 Gag and mice were challenged with vaccinia expressing Gag				
	• L. monocytogenes is a gram-positive bacteria that enters the macrophage on phagocytosis and lives in the cytoplasm – secreted L. monocytogenes antigens are processed and presented by both class I and class II pathways				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This article is a review of L. monocytogenes biology and its potential as a vaccine vector for HIV, comparing to other vector systems, and discussing CD4+ Th1 T-cells mediated Gag specific immunological protection in mice and the Gag CTL response				

III-B-5 RT Helper T-Cell Epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (36–52)	RT (36–52 BRU)	EICTEMEKEGKISKIGP	HIV-1 infection	human	De Groot1991
	• 9 out of 17 humans can make strong IL2 responses to this epitope				
RT (38–52)	RT (38–52 BRU)	CTEMEKEGKISKIGP	Vaccine	murine (H-2^k)	De Groot1991
	Vaccine *Vector/Type:* recombinant protein *Strain:* BRU *HIV component:* RT				
	• T-cells from RT immunized mice have enhanced proliferative response with peptide				
RT (39–53)	RT (194–208)	TEMEKEGKISKIGPE	in vitro stimulation	human	Manca1995a
	• Protein priming induced T-cells that recognize peptide, 4 clones from a single donor recognized this peptide				
RT (48–62)	RT (48–62 BRU)	SKIGPENPYNTPVFA	Vaccine	murine (H-2^k)	De Groot1991
	Vaccine *Vector/Type:* recombinant protein *Strain:* BRU *HIV component:* RT				
	• T-cells from RT immunized mice have enhanced proliferative response with peptide				
RT (62–77)	RT (62–77 BRU)	AIKKKDSTKWRKLVDF	Vaccine	murine (H-2^k)	De Groot1991
	Vaccine *Vector/Type:* recombinant protein *Strain:* BRU *HIV component:* RT				
	• T-cells from RT immunized mice have enhanced proliferative response with peptide				
RT (88–102)	RT (88–102 BRU)	WEVQLGIPHPAGLKK	Vaccine	murine (H-2^{t4})	De Groot1991
	Vaccine *Vector/Type:* recombinant protein *Strain:* BRU *HIV component:* RT				
	• T-cells from RT immunized mice have enhanced proliferative response with peptide				
RT (124–138)	Pol (303–317)	FRKYTAFTIPSINNE	HIV-1 infection	human (DR supermotif)	Wilson2001
	• Epitope name: Pol 303				
	• Eleven peptides were identified that had the HLA-DR supermotif, all were found to bind to MHC class II DR molecules and all elicited proliferative responses from multiple HIV-infected donors				
	• This epitope binds seven HLA-DR alleles: DRB1*0901, DRB1*0802, DRB1*0701, DRB1*0405, DRB1*0401, DRB1*1501 and DRB1*0101, with an IC_{50} threshold below 1,000 nM				
	• This epitope sequence is conserved in 68% of clade B isolates				
	• 8/22 HIV infected individuals responded to this epitope (13/22 responded to some of the DR supermotif epitopes, the 9 non-responder peptides tended to also not have recall responses to rec HIV-1 whole proteins)				
RT (124–138)	Pol (303–317)	FRKYTAFTIPSINNE	Vaccine	murine (I-Ab and HLA-DR)	Livingston2002
	Vaccine *Vector/Type:* DNA with CMV promotor, peptide *HIV component:* polyepitope *Adjuvant:* CFA				
	• Epitope name: Pol 303				
	• Four Th HIV epitopes presented by HLA-DR molecules were identified that also could be presented my murine class II molecule I-Ab, enabling testing of vaccine strategies of in H-2b mice.				
	• Responses to pooled peptides, polyepitope peptides in a linear construct or in a branched MAP construct, and a DNA polyepitope construct with a CMV promotor were compared. A linear arrangement in polyepitope construct created a junctional epitope that could be disrupted with the addition of GPGPG spacers. The linear polyepitope construct with the GPGPG spacer worked well in terms of eliciting responses to all four peptides, using either DNA or protein for the vaccination.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (133–147)	RT (133–147 BRU)	PSINNETPGIRYQYN	Vaccine	murine (H-$2^{k,i5}$)	De Groot1991
	Vaccine *Vector/Type:* recombinant protein *Strain:* BRU *HIV component:* RT • T-cells from RT immunized mice have enhanced proliferative response with peptide				
RT (144–158)	RT (144–158 BRU)	YQYNVLPQGWKGSPA	Vaccine	murine (H-2^{t4})	De Groot1991
	Vaccine *Vector/Type:* recombinant protein *Strain:* BRU *HIV component:* RT • T-cells from RT immunized mice have enhanced proliferative response with peptide				
RT (156–170)	Pol (335–349)	SPAIFQSSMTKILEP	HIV-1 infection	human (DR supermotif)	Wilson2001
	• Epitope name: Pol 596 • Eleven peptides were identified that had the HLA-DR supermotif, all were found to bind to MHC class II DR molecules and all elicited proliferative responses from multiple HIV-infected donors • This epitope binds nine HLA-DR alleles: DRB1*0101, DRB1*1501, DRB1*0405, DRB1*1101, DRB1*1302, DRB1*0701, DRB1*0901, DRB5*0101 and DRB3*0101, with an IC_{50} threshold below 1,000 nM • This epitope sequence is conserved in 79% of clade B isolates • 7/22 HIV infected individuals responded to this epitope (13/22 responded to some of the DR supermotif epitopes, the 9 non-responder peptides tended to also not have recall responses to rec HIV-1 whole proteins)				
RT (156–170)	Pol (335–449)	SPAIFQSSMTKILEP	Vaccine	murine (I-Ab and HLA-DR)	Livingston2002
	Vaccine *Vector/Type:* DNA with CMV promotor, peptide *HIV component:* polyepitope *Adjuvant:* CFA • Epitope name: Pol 335 • Four Th HIV epitopes presented by HLA-DR molecules were identified that also could be presented my murine class II molecule I-Ab, enabling testing of vaccine strategies of in H-2b mice. • Responses to pooled peptides, polyepitope peptides in a linear construct or in a branched MAP construct, and a DNA polyepitope construct with a CMV promotor were compared. A linear arrangement in polyepitope construct created a junctional epitope that could be disrupted with the addition of GPGPG spacers. The linear polyepitope construct with the GPGPG spacer worked well in terms of eliciting responses to all four peptides, using either DNA or protein for the vaccination.				
RT (171–190)	RT (171–190 HXB2)	FRKQNPDIVIYQYMDDLYVG	HIV-1 infection	human (DR1, 2 or 3, 4 and 7)	vanderBurg1999
	• T-cells specific for this epitope from the three donors were stimulated when presented with target cells pulsed with whole RT, indicating that the peptide is naturally processed for multiple HLA-DR molecules • Epitope binds to HLA-DR1, -DR2, -DR3, -DR4, and DR7, and can elicit Th1 cells that recognize peptide, protein, and HIV pulsed stimulator cells in the context of DR1, 2 or 3, 4 and 7 – these HLA types cover more than half of the general population				
RT (171–190)	RT (171–190 HXB2)	FRKQNPDIVIYQYMDDLYVG	HIV-1 infection, in vitro stimulation	human (DR1, DR2, DR3, DR4, DR7)	vanderBurg1999
	• The goal of this study was to identify Th epitopes that could be cross-presented by multiple class II HLA molecules. 5 RT peptides were identified that could bind to more than one HLA class II protein, and but only 2/5 could stimulate strong proliferation responses in PBMC derived from multiple healthy donors. • This highly conserved epitope binds with high affinity to HLA-DR1, -DR2, -DR3, -DR4, and -DR7 but not HLA-DR5, and stimulated proliferation in 3/3 PBMC individuals with the appropriate HLA alleles. • This epitope was able to be naturally processed in protein pulsed stimulator cells, and responding clones had a Th1 cytokine profile.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This epitope is highly conserved and spans the highly conserved YMDD motif, and showing only minor variability in clades A, B, and D.				
RT (195–209)	RT (IIIB)	IGQHRTKIEELRQHL	in vitro stimulation	human	Manca1995b
	• Protein priming induced T-cells that recognize peptide				
RT (196–215)	RT (351–370)	GQHRTKIEELRQHLLRWGLT	in vitro stimulation	human	Manca1995a
	• Protein priming induced T-cells that recognize peptide, 4 clones from a single donor recognized this peptide				
RT (249–263)	RT (IIIB)	KDSWTWNDIQKLVGK	in vitro stimulation	human	Manca1995b
	• Peptide stimulation of PBMC from non-infected individuals in vitro • Peptide priming did not induce T-cells that recognize whole protein				
RT (249–263)	RT (248–262)	KDSWTVNDIQKLVGK	in vitro stimulation	human	De Berardinis1999
	• PBMC from donors GD (HLA DR 11; DRB52) and LD (HLA DR 11, 13; DRB52) recognized this epitope (pep23) • A subset of T-cell lines generated from these donors were capable of recognizing pep23 expressed on the surface of filamentous phage fd, fused to the major coat protein gVIIIp • This peptide was selected to study phage presentation of peptide sequences because it was known to serve as a T-cell helper determinant which could induce proliferation from a naive repertoire [Manca1995a]				
RT (249–263)	RT (249–263)	KDSWTVNDIQKLVGK	Vaccine, in vitro stimulation	human (DR5)	De Berardinis2000
	Vaccine *Vector/Type:* HIV-1 peptide in filamentous bacteriophage major coat protein *HIV component:* RT peptides • Epitope name: RT2 • Phage display of the CTL epitope, ILKEPVHGV coupled with T helper epitope KDSWTVNDIQKLVGK, elicited specific CTL responses in PBMC from HIV negative individuals and in vivo in immunization of HLA-A2 transgenic mice • Bacteriophage presentation of peptides is generally used for stimulation of antibodies, and this novel discovery of CTL epitope processing and presentation suggests new possibilities for these vectors • HIV-1 peptides were displayed in filamentous bacteriophage fd virion major coat protein pVIII				
RT (249–263)	RT (248–262 HXB2)	KDSSTVNDIQKLVGK	in vitro stimulation	human (DRS)	Fenoglio1999
	• RT pep23 epitope exhibited antagonistic activity against proliferation of gp120-specific T-cells when flanked by unrelated amino acid sequence • The glutathione S-transferase (GST)-peptide system can be used to display peptides; antigenicity was maintained when this peptide was expressed at the C-term end, but antagonism resulted when this peptide was expressed at the N-term end				
RT (251–261)	RT (250–260)	SSTVNDIQKLV	in vitro stimulation	human (DR5(11.01))	Manca1996
	• This peptide was the minimal stimulatory sequence • One Th line was stimulated by p66, one by a Glutathione-S-transferase (GST)-peptide fusion protein • Constructs linking GST to the KDSSTVNDIQKLVGK peptide at the N-term end of GST stimulated Th cells, but not constructs linking at the C-term end • The C and N termini of GST are not intrinsically permissive or non-permissive, presentation is epitope specific (see FAILKCNNK for contrast)				
RT (258–272)	RT (IIIB)	QKLWGKLNWASQIYP	in vitro stimulation	human	Manca1995b
	• Peptide stimulation of PBMC from non-infected individuals in vitro • Peptide priming did not induce T-cells that recognize whole protein				
RT (271–290)	RT (271–290 HXB2)	YPGIKVRQLCKLLRGTKALT	HIV-1 infection	human	vanderBurg1999
	• Epitope can bind to at least 5 different HLA-DR molecules, and peptide on target cells can elicit Th responses from PBMC cultures from healthy donors, however it does not seem to be processed properly from whole RT or virus				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (271–290)	RT (271–290 HXB2)	YPGIKVRQLCKLLRGTKALT	HIV-1 infection, in vitro stimulation	human (DR1, DR2, DR3, DR5, DR7)	vanderBurg1999
	• The goal of this study was to identify Th epitopes that could be cross-presented by multiple class II HLA molecules. 5 RT peptides were identified that could bind to more than one HLA class II protein, but only 2/5 could stimulate strong proliferation responses in PBMC derived from multiple healthy donors. • This epitope binds with high affinity to HLA-DR1, -DR2, -DR3, -DR5, and -DR7 but not HLA-DR4, and stimulated proliferation in 3/4 individuals with the appropriate HLA alleles. • This epitope was not able to be naturally processed in protein-pulsed stimulator cells.				
RT (276–290)	RT (IIIB)	WRQLCKLLRGTKALT	in vitro stimulation	human	Manca1995b
	• Protein priming induced T-cells that recognize peptide				
RT (285–299)	RT (IIIB)	GTKALTEVIPLTEEA	in vitro stimulation	human	Manca1995b
	• Protein priming induced T-cells that recognize peptide				
RT (294–308)	RT (IIIB)	PLTEEAELELAENRE	in vitro stimulation	human	Manca1995b
	• Protein priming induced T-cells that recognize peptide				
RT (303–317)	RT (IIIB)	LAENREILKEPVHGV	in vitro stimulation	human	Manca1995b
	• Protein priming induced T-cells that recognize peptide				
RT (384–398)	RT (IIIB)	GKTPKFKLPIQKETW	in vitro stimulation	human	Manca1995b
	• Protein priming induced T-cells that recognize peptide				
RT (414–428)	Pol (596–610)	WEFVNTPPLVKLWYQ	HIV-1 infection	human (DR supermotif)	Wilson2001
	• Epitope name: Pol 596 • Eleven peptides were identified that had the HLA-DR supermotif, all were found to bind to MHC class II DR molecules and all elicited proliferative responses from multiple HIV-infected donors • This epitope binds eleven HLA-DR alleles: DRB1*0101, DRB1*1501, DRB1*0401, DRB1*0405, DRB1*1101, DRB1*1302, DRB1*0701, DRB1*0802, DRB1*0901, DRB5*0101 and DRB4*0101, with an IC_{50} threshold below 1,000 nM • This epitope sequence is conserved in 84% of clade B isolates • 6/22 HIV infected individuals responded to this epitope (13/22 responded to some of the DR supermotif epitopes, the 9 non-responder peptides tended to also not have recall responses to rec HIV-1 whole proteins)				
RT (429–443)	RT (IIIB)	LEKEPIVGAETFYVD	in vitro stimulation	human	Manca1995b
	• Protein priming induced T-cells that recognize peptide				
RT (432–450)	RT (431–450 HXB2)	EPIVGAETFYVDGAANRET	HIV-1 infection, in vitro stimulation	human (DR1, DR2, DR3, DR4)	vanderBurg1999
	• The goal of this study was to identify Th epitopes that could be cross-presented by multiple class II HLA molecules. 5 RT peptides were identified that could bind to more than one HLA class II protein, and but only 2/5 could stimulate strong proliferation responses in PBMC derived from multiple healthy donors. • This epitope binds with high affinity to HLA-DR1, -DR2, -DR3, and -DR4, but stimulated a strong proliferation response in only 1/4 individuals tested so was not considered broadly cross-presented.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (526–540)	RT (526–540 BRU)	IKKEKVYLAWVPAHK	Vaccine	murine (Ad or Dd)	Haas1991
	Vaccine *Vector/Type:* peptide, inactivated virus, recombinant protein *Strain:* BRU *HIV component:* whole virus, RT *Adjuvant:* CFA • Epitope name: W9 • Of 5 mouse inbred lines tested: DBA/2 (H-2d, Ad, Ed), B10.A(4R) (H-2h4, Ak) and B10.A(5R) (H-2i5) showed particularly good CD4+ T cell proliferative responses to HIV proteins (gp160, gp120, p17, p24, Nef and RT), after vaccination with inactivated virus. • B10.BR (H-2k, Ak, Ek) and C57BL/6 (H-2b and Ab) had weaker responses. • The peptide KEKVYLAWVPAHKG was one of two RT peptides with Th cells recognition.			
RT (528–541)	RT (528–543 BRU)	KEKVYLAWVPAHKG	Vaccine	murine (Ad and Dd)	Haas1991
	Vaccine *Vector/Type:* peptide, inactivated virus, recombinant protein *Strain:* BRU *HIV component:* whole virus, RT *Adjuvant:* CFA • Epitope name: A3 • Of 5 mouse inbred lines tested: DBA/2 (H-2d, Ad, Ed), B10.A(4R) (H-2h4, Ak) and B10.A(5R) (H-2i5) showed particularly good CD4+ T cell proliferative responses to HIV proteins (gp160, gp120, p17, p24, Nef and RT), after vaccination with inactivated virus. • B10.BR (H-2k, Ak, Ek) and C57BL/6 (H-2b and Ab) had weaker responses. • The peptide KEKVYLAWVPAHKG was one of two RT peptides with Th cells recognition. It could by itself prime different strains of mice for RT-specific Th responses, and the C-term half of the peptide is highly conserved in HIV-1, HIV-2 and SIV strains.			
RT (528–543)	RT (528–543 BRU)	KEKVYLAWVPAHKGIG	Vaccine	murine (H-$2^{f,k,d}$)	Haas1991
	Vaccine *Vector/Type:* peptide *Strain:* BRU • T-cells from peptide-primed mice could be restimulated by native RT				
RT (529–543)	Pol (711–725)	EKVYLAWVPAHKGIG	HIV-1 infection	human (DR supermotif)	Wilson2001
	• Epitope name: Pol 711 • Eleven peptides were identified that had the HLA-DR supermotif, all were found to bind to MHC class II DR molecules and all elicited proliferative responses from multiple HIV-infected donors • This epitope binds ten HLA-DR alleles: DRB1*0101, DRB1*1501, DRB1*0401, DRB1*0405, DRB1*1101, DRB1*0701, DRB1*0802, DRB1*0901, DRB5*0101 and DRB4*0101, with an IC_{50} threshold below 1,000 nM • This epitope sequence is conserved in 94% of clade B isolates • 6/22 HIV infected individuals responded to this epitope (13/22 responded to some of the DR supermotif epitopes, the 9 non-responder peptides tended to also not have recall responses to rec HIV-1 whole proteins)			
RT (529–543)	Pol (711–725)	EKVYLAWVPAHKGIG	Vaccine	murine (I-Ab and HLA-DR)	Livingston2002
	Vaccine *Vector/Type:* DNA with CMV promotor, peptide *HIV component:* polyepitope *Adjuvant:* CFA • Epitope name: Pol 711 • Four Th HIV epitopes presented by HLA-DR molecules were identified that also could be presented my murine class II molecule I-Ab, enabling testing of vaccine strategies of in H-2b mice. • Responses to pooled peptides, polyepitope peptides in a linear construct or in a branched MAP construct, and a DNA polyepitope construct with a CMV promotor were compared. A linear arrangement in polyepitope construct created a junctional epitope that could be disrupted with the addition of GPGPG spacers. The linear polyepitope construct with the GPGPG spacer worked well in terms of eliciting responses to all four peptides, using either DNA or protein for the vaccination. • Although responses to this peptide indicated it was immunodominant, responses to all four peptides were made upon vaccination with linear constructs when GPGPG spacers were used.			

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (530–544)	Pol (712–726)	KVYLAWVPAHKGIGG	HIV-1 infection	human (DR supermotif)	Wilson2001

- Epitope name: Pol 712
- Eleven peptides were identified that had the HLA-DR supermotif, all were found to bind to MHC class II DR molecules and all elicited proliferative responses from multiple HIV-infected donors
- This epitope binds ten HLA-DR alleles: DRB1*0101, DRB1*1501, DRB1*0401, DRB1*0405, DRB1*1101, DRB1*0701, DRB1*0802, DRB1*0901, DRB5*0101 and DRB4*0101, with an IC_{50} threshold below 1,000 nM
- This epitope sequence is conserved in 89% of clade B isolates
- 6/22 HIV infected individuals responded to this epitope (13/22 responded to some of the DR supermotif epitopes, the 9 non-responder peptides tended to also not have recall responses to rec HIV-1 whole proteins)

III-B-6 RT-Integrase Helper T-Cell Epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT-Integrase (553–3)	RT (720–730 LAI) • Stimulates T-cell proliferation in HIV-infected donors	SAGIRKVLFLD	HIV-1 infection	human	Schrier1989

III-B-7 Integrase Helper T-Cell Epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Integrase (16–30)	Pol (758–772) • Epitope name: Pol 758 • Eleven peptides were identified that had the HLA-DR supermotif, all were found to bind to MHC class II DR molecules and all elicited proliferative responses from multiple HIV-infected donors • This epitope binds eight HLA-DR alleles: DRB4*0101, DRB5*0101, DRB1*0901, DRB1*0701, DRB1*1101, DRB1*0405, DRB1*0401 and DRB1*0101, with an IC_{50} threshold below 1,000 nM • This epitope sequence is conserved in 68% of clade B isolates • 8/22 HIV infected individuals responded to this epitope (13/22 responded to some of the DR supermotif epitopes, the 9 non-responder peptides tended to also not have recall responses to rec HIV-1 whole proteins)	HSNWRAMASDFNLPP	HIV-1 infection	human (DR supermotif)	Wilson2001
Integrase (172–186)	RT (899–913 LAI) • Stimulates T-cell proliferation in HIV-infected donors	LKTAVQMAVFIHNFK	HIV-1 infection	human	Schrier1989
Integrase (173–187)	Pol (915–929) • Epitope name: Pol 915 • Eleven peptides were identified that had the HLA-DR supermotif, all were found to bind to MHC class II DR molecules and all elicited proliferative responses from multiple HIV-infected donors • This epitope binds seven HLA-DR alleles: DRB5*0101, DRB1*1302, DRB1*1101, DRB1*0405, DRB1*0401, DRB1*1501 and DRB1*0101, with an IC_{50} threshold below 1,000 nM • This epitope sequence is conserved in 94% of clade B isolates • 6/22 HIV infected individuals responded to this epitope (13/22 responded to some of the DR supermotif epitopes, the 9 non-responder peptides tended to also not have recall responses to rec HIV-1 whole proteins)	KTAVQMAVFFIHNFKR	HIV-1 infection	human (DR supermotif)	Wilson2001
Integrase (196–210)	RT (923–937 LAI) • Stimulates T-cell proliferation in HIV-infected donors	AGERIVDIIATDIQT	HIV-1 infection	human	Schrier1989
Integrase (214–228)	Pol (956–970) • Epitope name: Pol 956 • Eleven peptides were identified that had the HLA-DR supermotif, all were found to bind to MHC class II DR molecules and all elicited proliferative responses from multiple HIV-infected donors • This epitope binds twelve HLA-DR alleles: DRB4*0101, DRB5*0101, DRB1*0901, DRB1*0802, DRB1*0701, DRB1*1302, DRB1*1201, DRB1*1101, DRB1*0405, DRB1*0401, DRB1*1501 and DRB1*0101, with an IC_{50} threshold below 1,000 nM • This epitope sequence is conserved in 95% of clade B isolates • 8/22 HIV infected individuals responded to this epitope (13/22 responded to some of the DR supermotif epitopes, the 9 non-responder peptides tended to also not have recall responses to rec HIV-1 whole proteins)	QKQITKIQNFRVYYR	HIV-1 infection	human (DR supermotif)	Wilson2001
Integrase (215–227)	RT (942–954 LAI) • Stimulates T-cell proliferation in HIV-infected donors	KQITKIQNFRVYY	HIV-1 infection	human	Schrier1989

III-B-8 Pol Helper T-Cell Epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Pol	Gag/Pol		Vaccine	murine	Kim1997b
	Vaccine *Vector/Type:* DNA *HIV component:* GAG, POL, VIF *Adjuvant:* B7 and IL-12 expression vector				
	• A gag/pol DNA vaccine delivered in conjunction with the plasmid encoding the co-stimulatory molecules B7 and IL-12 gives a dramatic increase in both the cytotoxic and proliferative responses in mice				
Pol	Gag/Pol		Vaccine	murine	Kim1997d
	Vaccine *Vector/Type:* DNA *HIV component:* gp160, GAG, POL *Adjuvant:* CD86 expression vectors				
	• A gag/pol DNA vaccine delivered in conjunction with the plasmid encoding the co-stimulatory molecule CD86 gives an increase in proliferative responses to Pr55 in mice				
Pol	Gag/Pol (MN)		Vaccine	chimpanzee	Kim1998
	Vaccine *Vector/Type:* DNA *Strain:* MN *HIV component:* GAG, POL, ENV *Adjuvant:* CD80 and CD86 expression vectors				
	• Co-stimulatory molecules co-expressed with an HIV-1 immunogen in a DNA vaccine used to enhance the immune response – co-expression of CD86, but not CD80, dramatically increased both HIV Env and Gag/Pol specific CTL and Th proliferative responses				
Pol	Pol		HIV-1 infection	human	Blankson2001a
	• 5/10 chronically HIV infected patients with low CD4+ counts who received HAART therapy and experienced immune reconstitution displayed p24, p17 and p66 T-helper CD4 proliferative responses, in contrast to 0/8 chronically HIV infected patients with high CD4+ counts at the initiation of antiretroviral treatment				
	• This surprising result could be due to the low CD4 nadir patients being more likely to have thymic regeneration or a peripheral expansion of T cells				
Pol	p66		HIV-1 infection	human	Oxenius2000
	• Patients who started therapy at acute HIV infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable				
Pol	p66		HIV-1 infection	human	Palmer2002
	• CD4+ T cell proliferative responses from 33 HIV-1 infected patients with HAART suppression were compared to 19 patients with active viral replication (HAART failures and HAART naive). Patients with HAART suppression showed stronger p24- and p66-specific proliferative responses compared to patient groups with active HIV-1 replication, suggesting active viral replication in vivo specifically reduces proliferation responses.				
	• No differences in the frequency of HIV-specific CD4+ T-cells that were positive for cytokine secretion in a flow cytometry assay were found in the HAART suppressed group versus the group with active viral replication.				
Pol	(BRU)		Vaccine	murine	Haas1991
	Vaccine *Vector/Type:* inactivated virus *Strain:* BRU *HIV component:* whole virus, RT *Adjuvant:* Freund's adjuvant (CFA)				
	• Of 5 mouse inbred lines tested DBA/2 (H-2d, Ad, Ed), B10.A(4R) (H-2h4, Ak) and B10.A(5R) (H-2i5) showed particularly good CD4+ T cell proliferative responses to HIV proteins (gp160, gp120, p17, p24, Nef and RT), after vaccination with inactivated virus.				
	• B10.BR (H-2k, Ak, Ek) and C57BL/6 (H-2b and Ab) had weaker responses.				
Pol	RT (248–256 HXB2)		in vitro stimulation	human (DR5)	Manca1995b
	• CD4+ T-cell lines from uninfected individuals by stimulation with p66-pulsed APC				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• TcR Vβ Dβ Jβ sequences were obtained from p66-specific T-cell clones • There were multiple responses to peptides throughout p66, but because of uncertain locations, they have not been mapped • Response to peptide 248-256 was associated with DR5				
Pol	RT		Vaccine	murine (H-2^d)	Kim2000
	Vaccine *Vector/Type:* DNA *HIV component:* GAG, POL, ENV *Adjuvant:* IL-2, IL-4 and IFNγ expression vectors • Co-stimulatory molecules co-expressed with an HIV-1 immunogen in a DNA vaccine used to enhance the immune response – co-expression of Th1 cytokine IFN-gamma drove Th1 immune responses and enhanced CTL responses				
Pol	RT		Vaccine	murine (H-2^d)	Burnett2000
	Vaccine *Vector/Type:* Salmonella *HIV component:* RT epitope • A live attenuated bacterial vaccine, Salmonella SL3261-pHART, with an inserted HIV RT gene in the Lpp-OmpA-HIV fusion protein, induced a lymphoproliferative Th response in BALB/c mice				

III-B-9 Vif Helper T-Cell Epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Vif (65–76)	Vif (65–80) • T-cell response to this epitope persisted after seroreversion	VITTYWGLHTGE	HIV-1 infection	human	Ranki1997
Vif (81–96)	Vif (81–96) • T-cell response to this epitope persisted after seroreversion	LGQGVSIEWRKQRYST	HIV-1 infection	human	Ranki1997
Vif	Vif **Vaccine** *Vector/Type:* DNA *HIV component:* Vif, Vpu, Nef • Splenocytes from BALB/c mice immunized with pVVN-P DNA were incubated with Vif, Vpu or Nef antigens for 3 days and assayed for IL-4 and IFN-gamma levels • Antigen stimulation increased IFN-gamma production in pVVN-P immunized mice, indicating a Th1 response • IL-4 production was not significantly changed after antigen stimulation compared to control levels • Cross-clade CTL activity was also observed: A, B clade, CRF01(AE) clade antigens could serve as targets for the B clade immunization stimulated CTL – an HIV-1 AC recombinant, however, did not stimulate a CTL response, but was expressed at lower levels on the target cell		Vaccine	murine (H-2^d)	Ayyavoo2000

III-B-10 Vpr Helper T-Cell Epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Vpr (66–80)	Vpr (66–80 IIIB)	QLLFIHFRIGCRHSR	HIV-1 infection	human	Sarobe1994
	• This peptide was found to stimulate proliferative responses in 37.5% of HIV-1 positive individuals				
Vpr (66–80)	Vpr (66–80 IIIB)	QLLFIHFRIGCRHSR	Vaccine	murine (H-2^d)	Sarobe1994
	Vaccine *Vector/Type:* peptide				
	• Included as a Th stimulatory component of peptide vaccines that also incorporated B-cell epitopes				

III-B-11 Tat Helper T-Cell Epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Tat (1–20)	Tat (1–20 LAI)	MEPVDPRLEPWKHPGSQPKT	Vaccine	murine (H-2^d)	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* LAI *HIV component:* NEF, TAT, REV • Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein • Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev				
Tat (16–35)	Tat (16–35 LAI)	SQPKTACTTCYCKKCCFHCQ	Vaccine	murine (H-2^d)	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* LAI *HIV component:* NEF, TAT, REV • Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein • Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev				
Tat (17–32)	Tat (17–32)	QPKTACTNCYCKRCCF	HIV-1 infection	human	Ranki1997
	• T-cell response to this epitope persisted after seroreversion				
Tat (17–32)	Tat (17–32 HXB2)	QPKTACTNCYCKKCCF	HIV-1 infection	human (DR5? plus others)	Blazevic1993
	• Epitope name: D26 • 9/14 (64%) of HIV-1 positive patients had proliferative T-cell responses associated with IL-2 production against at least one Tat-derived synthetic peptides of twelve overlapping 15-16 mer peptides spanning Tat. T cell proliferation was associated with IL-2 production. • 3/12 peptides were recognized. • This immunodominant, highly conserved and most frequently recognized peptide was recognized by 57% of the HIV-1 infected patients. A beta-sheet secondary structure was predicted at aa residues 21-28, but no amphipathic helix structure, suggested to be most favorable for T-cell epitopes, was indicated. • This peptide contained epitopes restricted by several HLA DR alleles, although the frequency of DR5 was enriched (3/6) among the patients that recognized the peptide.				
Tat (31–50)	Tat (31–50 LAI)	CFHCQVCFTTKALGISYGRK	Vaccine	murine (H-2^d)	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* LAI *HIV component:* NEF, TAT, REV • Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein • Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev				
Tat (33–48)	Tat (33–48)	HCQVCFMTKGLGISYG	HIV-1 infection	human	Ranki1997
	• T-cell response to this epitope persisted after seroreversion				
Tat (33–48)	Tat (33–48 HXB2)	HCQVCFITKALGISYG	HIV-1 infection	human (DR5? plus others)	Blazevic1993
	• Epitope name: D28 • 9/14 (64%) of HIV-1 positive patients had proliferative T-cell responses associated with IL-2 production against at least one Tat-derived synthetic peptides of twelve overlapping 15-16 mer peptides spanning Tat. T cell proliferation was associated with IL-2 production. • 3/12 peptides were recognized. • 4/14 HIV+ people recognized this peptide. • An alpha-helix structure was predicted at residues 39-44, but charge patterns did not indicate it was an amphipathic helix, suggested to be most favorable for T-cell epitopes.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This peptide contained epitopes restricted by several HLA DR alleles, although the frequency of DR5 was enriched (2/4) among the patients that recognized the peptide.				
Tat (46–65)	Tat (46–65 LAI)	SYGRKKRRQRRRPPQGSQTH	Vaccine	murine (H-2^d)	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* LAI *HIV component:* NEF, TAT, REV • Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein • Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev				
Tat (61–80)	Tat (61–80 LAI)	GSQTHQVSLSKQPTSQPRGD	Vaccine	murine (H-2^d)	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* LAI *HIV component:* NEF, TAT, REV • Stronger, broader responses were observed in animals vaccinated with DNA epidermally; rather than with intramuscular protein • Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev				
Tat (65–80)	Tat (65–80 HXB2)	HQASLSKQPTSQPRGD	HIV-1 infection	human (DR2? plus others)	Blazevic1993
	• Epitope name: D32 • 9/14 (64%) of HIV-1 positive patients had proliferative T-cell responses associated with IL-2 production against at least one Tat-derived synthetic peptides of twelve overlapping 15-16 mer peptides spanning Tat. T cell proliferation was associated with IL-2 production. • 3/12 Tat peptides were recognized. • 3/14 HIV+ people recognized this peptide. • An alpha-helix structure was predicted at residues 65-72, but charge patterns did not indicate it was an amphipathic helix, suggested to be most favorable for T-cell epitopes.. • This peptide contained epitopes restricted by several HLA DR alleles, although the frequency of DR2 was enriched (2/3) among the patients that recognized the peptide.				
Tat (67–86)	Tat (67–86 LAI)	VSLSKQPTSQPRGDPTGPKE	Vaccine	murine (H-2^d)	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* LAI *HIV component:* NEF, TAT, REV • Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein • Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev				
Tat	Tat		Vaccine	human	Calarota1999
	Vaccine *Vector/Type:* DNA *HIV component:* NEF, REV, TAT • 9/9 HIV-1+ subjects were given one of three DNA vaccinations for nef, rev or tat, and novel proliferative and CTL responses were generated • The nef DNA immunization induced the highest and most consistent CTLp activity, IFN-gamma production, and IL-6 and IgG responses • Highly active antiretroviral treatment (HAART) did not induce new HIV-specific CTL responses but reduced viral load, while DNA vaccination induced new immune responses but did not reduce viral load – thus this is a potentially complementary and promising combination				
Tat	Tat		HIV-1 infection, Vaccine	human	Calarota2001
	Vaccine *Vector/Type:* DNA *HIV component:* Nef, Rev, Tat *Adjuvant:* CpG motifs • This review discusses the cellular immune response, and comments on CpG induction of Th1 cytokines and enhanced immune responses, and HIV-1 DNA vaccine boosting of CTL and Th proliferative responses in asymptomatic HIV+ individuals				
Tat	Tat		in vitro stimulation	human	Corinti2002
	• In vitro delivery of recombinant Tat protein conjugated to red blood cells (RBCs) via avidin-biotin bridges (RBC-Tat) to human dendritic cells was compared to dendritic cells pulsed with rec Tat.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Dendritic cells pulsed with RBC-Tat elicited specific and significantly stronger CD4+ and CD8+ T-cell responses and required 1250-fold less antigen than DCs stimulated with soluble Tat. • Dendritic cells which were maturated in the presence of IFNgamma induced elevated IL-12 and TNF-alpha secretion. IFNgamma upregulated IP-10 and down regulated TARC, chemokines which attract Th1 and Th2 cells, respectively.				
Tat	Tat (IIIB, BH10)		in vitro stimulation	human	Fanales-Belasio2002
	• Biologically active HIV-1 Tat is readily taken up by monocyte-derived dendritic cells (MDDC) (and activated endothelial cells), but not other APCs. Tat must be in a native, non-oxidized conformation for efficient uptake. Tat upregulates MHC molecules, IL-12, TNFα, RANTES and MIP-1-α and MIP-1-β production which drives Th1 immune responses and enhances antigen presentation. • Native Tat enhanced the antigen presentation of MDDC and boosted proliferative recall and allogeneic antigen responses, and the authors propose it could be used as an adjuvant to drive the immune response as well as an antigen.				
Tat	Tat		Vaccine	murine (H-2^d)	Billaut-Mulot2001
	Vaccine *Vector/Type:* DNA with DNA boost, DNA with recombinant protein boost *Strain:* LAI *HIV component:* Gag, Tat, Nef *Adjuvant:* IL18 • DNA vaccinated BALB/c mice primed and boosted with a multiepitopic vaccine with IL18 gave lymphoproliferative responses 7 weeks post immunization • Strong but non-lasting HIV-specific CTL responses were detected by a Cr-release assay and DNA prime + DNA boost was more effective than DNA prime + protein boost • Immunization with either the multiepitopic DNA or with the mixed DNA vaccine resulted in Th1 cytokines production (IL-2 and IFNγ) in spleen cell cultures stimulated by Tat and Gag, while Th2 cytokines IL-4 and IL-10 production was not detectable • Co-administration of IL18 increased T-cell responses but decreased anti-HIV antibody levels				

III-B-12 Rev Helper T-Cell Epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Rev (9–23)	Rev (9–23 HXB2)	DEELIRTVRLIKLLY	HIV-1 infection	human	Blazevic1995
	• One of four peptides that stimulates in PBLs from HIV-1+ donors both CD4+ Th cell proliferation and CTL to autologous targets incubated with peptide were stimulated				
Rev (16–35)	Rev (16–35 LAI)	VRLIKFLYQSNPPPNPEGTR	Vaccine	murine (H-2^d)	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* LAI *HIV component:* NEF, TAT, REV				
	• Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein				
	• Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev				
Rev (25–39)	Rev (25–39 HXB2)	SNPPPNPEGTRQARR	HIV-1 infection	human	Blazevic1995
	• One of four peptides that stimulates in PBLs from HIV-1+ donors both CD4+ Th cell proliferation and CTL to autologous targets incubated with peptide were stimulated				
Rev (31–50)	Rev (31–50 LAI)	PEGTRQARRNRRRRWRERQR	Vaccine	murine (H-2^d)	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* LAI *HIV component:* NEF, TAT, REV				
	• Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein				
	• Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev				
Rev (33–48)	Rev (33–48 HXB2)	GTRQARRNRRRRWRER	HIV-1 infection	human	Blazevic1995
	• One of four peptides that stimulates in PBLs from HIV-1+ donors both CD4+ Th cell proliferation and CTL to autologous targets incubated with peptide were stimulated				
Rev (41–56)	Rev (41–56 HXB2)	RRRRWRERQRQIHSIS	HIV-1 infection	human	Blazevic1995
	• One of four peptides that stimulates in PBLs from HIV-1+ donors both CD4+ Th cell proliferation and CTL to autologous targets incubated with peptide were stimulated				
Rev (76–95)	Rev (76–95 LAI)	PPLERLTLDCNEDCGTSGTQ	Vaccine	murine (H-2^b)	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* LAI *HIV component:* NEF, TAT, REV				
	• Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein				
	• Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev				
Rev (96–116)	Rev (96–116 LAI)	GVGSPQILVESPTVLESGT-KE	Vaccine	murine (H-2^d)	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* LAI *HIV component:* NEF, TAT, REV				
	• Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein				
	• Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev				
Rev	Rev		Vaccine	murine	Chan1998
	Vaccine *Vector/Type:* DNA *HIV component:* REV				
	• Rev M10 is a construct that was introduced into mice through a genetic vaccination				
	• Rev was used to test for down-regulation of HIV-1 in infected cells as a method for gene therapy – in the course of this study, Rev-specific IL-2 producing Th cells developed in the mice				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Rev	Rev		Vaccine	human	Calarota1999
	Vaccine *Vector/Type:* DNA *HIV component:* Nef, Rev Tat • 9/9 HIV-1+ subjects were given one of three DNA vaccinations for nef, rev or tat, and novel proliferative and CTL responses were generated • The nef DNA immunization induced the highest and most consistent CTLp activity, IFN-gamma production, and IL-6 and IgG responses • Highly active antiretroviral treatment (HAART) did not induce new HIV-specific CTL responses but reduced viral load, while DNA vaccination induced new immune responses but did not reduce viral load – thus this is a potentially complementary and promising combination				
Rev	Rev		HIV-1 infection, Vaccine	human	Calarota2001
	Vaccine *Vector/Type:* DNA *HIV component:* Nef, Rev, Tat *Adjuvant:* CpG motifs • This review discusses the cellular immune response, and comments on CpG induction of Th1 cytokines and enhanced immune responses, and HIV-1 DNA vaccine boosting of CTL and Th proliferative responses in asymptomatic HIV+ individuals				
Rev	Rev		Vaccine	human	MacGregor2002
	Vaccine *Vector/Type:* DNA with CMV promotor *Strain:* MN *HIV component:* Env, Rev *Adjuvant:* bupivacaine • A phase I clinical trial of a HIV-1 Env and Rev DNA vaccine with a CMV promoter was conducted and Th proliferative, CTL and Elispot responses monitored. The construct was modified for safety and included no LTRs or packaging signals. The vaccine strategy was safe, and elicited strong CD4-T cell responses, but not CD8 T-cell responses. Rev elicited strong Th responses, and is a early produced protein so may confer advantages. • With a 300 ug dose, 4/6 individuals had a lymphocyte proliferation (LP) responses to gp120, 3/6 to Rev. • With a 1000 ug dose, 4/6 individuals had a LP and 2/6 had IFNgamma Elispot responses to gp160; 3/6 had LP, and 4/6 had IFNgamma Elispot responses to Rev. • No responses to three specific CTL epitopes were observed by Elispot in individuals with appropriate HLA. Some cytoxic activity against whole protein was observed that was CD4+ T-cell mediated.				

III-B-13 Vpu Helper T-Cell Epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Vpu (19–34)	Vpu (19–34)	AIVVWSIVLIEYRKIL	HIV-1 infection	human	Ranki1997
	• T-cell response to this epitope persisted after seroreversion				
Vpu	Vpu		Vaccine	murine (H-2^d)	Ayyavoo2000
	Vaccine *Vector/Type:* DNA *HIV component:* Vif, Vpu, Nef • Splenocytes from BALB/c mice immunized with pVVN-P DNA were incubated with Vif, Vpu or Nef antigens for 3 days and assayed for IL-4 and IFN-gamma levels • Antigen stimulation increased IFN-gamma production in pVVN-P immunized mice, indicating a Th1 response • IL-4 production was not significantly changed after antigen stimulation compared to control levels • Cross-clade CTL activity was also observed: A, B clade, CRF01(AE) clade antigens could serve as targets for the B clade immunization stimulated CTL – an HIV-1 AC recombinant, however, did not stimulate a CTL response, but was expressed at lower levels on the target cell			

III-B-14 gp160 Helper T-Cell Epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (30–51)	gp120 (30–51 IIIB)	ATEKLWVTVYYGVPVWKEA-TTT?	HIV-1 infection	human	Geretti1994
	• Epitope name: A1 • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 2/15 responders recognized this peptide, mean SI = 4.6.				
gp160 (32–44)	gp120 (39–51)	EQLWVTVYYGVPV	Vaccine	murine (H-2^{bxk})	Sastry1991
	Vaccine *Vector/Type:* peptide • Peptides induced T-cell proliferative response to immunizing peptide and to gp160				
gp160 (38–48)	Env (45–55)	VYYGVPVWKEA	Vaccine	Rhesus macaque	Nehete1993
	Vaccine *Vector/Type:* peptide • Synthetic peptide derived from conserved region of the HIV-1 envelope that stimulates a proliferative response in mice • Proliferative response to this peptide was observed in 3/3 immunized rhesus monkeys				
gp160 (38–48)	Env (45–55)	VYYGVPVWKEA	HIV-1 infection	human, chimpanzee	Nehete1998b
	• Seven out of nine HIV-infected chimpanzees and eight out of seventeen HIV-positive humans exhibited positive proliferative responses to this conserved peptide (peptide 104) – no HIV negative individuals showed a response • This peptide, along with 4 other peptides from conserved regions of envelope, can induce proliferative responses to HIV and may be useful for vaccines • Peptide 104 elicited proliferative responses in inbred mouse strains and outbred rhesus monkeys in previous study by same group				
gp160 (38–48)	gp120 (45–55)	VYYGVPVWKEA	Vaccine	murine (H-$2^{bxk,sxd}$)	Sastry1991
	Vaccine *Vector/Type:* peptide • Peptides induced T-cell proliferative response to immunizing peptide and to gp160				
gp160 (41–54)	Env (48–60)	GVPVWKEATTLFC	Vaccine	Rhesus macaque	Nehete1993
	Vaccine *Vector/Type:* peptide • Synthetic peptide derived from conserved region of the HIV-1 envelope that stimulates a proliferative response in mice • Despite the proliferative response to this peptide in mice, no response was observed in 3 rhesus monkeys				
gp160 (41–54)	gp120 (48–61)	GVPVWKEATTLFC	Vaccine	murine (H-2^{sxd})	Sastry1991
	Vaccine *Vector/Type:* peptide • Peptides induced T-cell proliferative response to immunizing peptide and to gp160				
gp160 (41–60)	gp120 (40–59 89.6)	GVPVWREATTTLFCASDAKA	Vaccine	murine	Dai2001
	Vaccine *Vector/Type:* recombinant protein *Strain:* 89.6 *HIV component:* gp120 *Adjuvant:* R192G mutant heat-labile toxin from enterotoxigenic E. coli (mLT) • Epitope name: Peptide 2				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences. • This peptide was highly reactive in 10/10 BALB/c mice tested, but only in 5/10 CBA/J mice.				
gp160 (41–60)	gp120 (40–59 89.6)	GVPVWREATTTLFCASDAKA	Vaccine	murine (H-2^d)	Dai2001
	Vaccine *Vector/Type:* recombinant protein *Strain:* 89.6 *HIV component:* gp120 *Adjuvant:* mutant R192G heat-labile toxin from E. coli as adjuvant • Promiscuous immunodominant epitopes in gp120 were mapped by overlapping peptides in CBA/J H-2^k and BALB/c H-2^d mice, and all were found to be in the outer domain, proximal to regions of structural disorder indicated by the crystal structure or by sequence divergence. • This peptide was recognized by 10/10 BALB/c with an average SI of 6.4, the strongest reaction among BALB/c mice, but not by CBA/J mice, but recognized well not by CBA/J mice, so is considered to be uniquely immunodominant for H-2^d • Uniquely immunodominant sequences tended to be in the inner domain of the protein				
gp160 (42–61)	gp120 (42–61 IIIB)	VPVWKEATTTLFCASDAKA-Y?	HIV-1 infection	human	Geretti1994
	• Epitope name: A2 • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 2/15 responders recognized this peptide, mean SI = 6.6.				
gp160 (52–71)	gp120 (52–71 IIIB)	LFCASDAKAYDTEVHNVWA-T?	HIV-1 infection	human	Geretti1994
	• Epitope name: A3 • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 3/15 responders recognized this peptide, mean SI = 4.3.				
gp160 (61–80)	gp120 (60–79 89.6)	YDTEVHNVWATHACVPTDPN	Vaccine	murine	Dai2001
	Vaccine *Vector/Type:* recombinant protein *Strain:* 89.6 *HIV component:* gp120 *Adjuvant:* R192G mutant heat-labile toxin from enterotoxigenic E. coli (mLT) • Epitope name: Peptide 4 • Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences. • This peptide was highly reactive in 4/10 BALB/c mice tested, but only in 1/10 CBA/J mice.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (62–80)	gp120 (62–80 IIIB)	DTEVHNVWATHACVPTDPN?	HIV-1 infection	human	Geretti1994
	• Epitope name: A4 • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 1/15 responders recognized this peptide, SI = 3.5.				
gp160 (65–75)	gp120 (72–82)	AHKVWATHACV	Vaccine	murine (H-$2^{bxk,sxd}$)	Sastry1991
	Vaccine *Vector/Type:* peptide • Peptides induced T-cell proliferative response to immunizing peptide and to gp160				
gp160 (74–85)	gp120 (74–85 LAI)	CVPTDPNPQEVV	HIV-1 infection	human	Schrier1989
	• Stimulates T-cell proliferation in HIV-infected donors				
gp160 (74–85)	gp120 (81–92)	CVPTNPVPQEVV	Vaccine	murine (H-$2^{bxk,sxd}$)	Sastry1991
	Vaccine *Vector/Type:* peptide • Peptides induced T-cell proliferative response to immunizing peptide and to gp160				
gp160 (80–99)	gp120 (51–70 HXB2)	NPQEVVLVNTENFNMWKND	in vitro stimulation	human	Li Pira1998
	• Clonal heterogeneity was broad for a recall response to tetanus toxoid or PPD, but oligoclonal to primary HIV antigens, dominated in this case by TCR Vβ 13 usage • Donor of PBMC that recognized this epitope had HLA-DR alleles 2 and 7				
gp160 (81–100)	gp120 (80–99 89.6)	PQEVVLGNVTENFNMWKNNM	Vaccine	murine	Dai2001
	Vaccine *Vector/Type:* recombinant protein *Strain:* 89.6 *HIV component:* gp120 *Adjuvant:* R192G mutant heat-labile toxin from enterotoxigenic E. coli (mLT) • Epitope name: Peptide 6 • Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences. • This peptide was not reactive in any BALB/c mice tested (0/10), but was highly reactive in all (10/10) CBA/J mice.				
gp160 (81–100)	gp120 (80–99 89.6)	PQEVVLGNVTENFNMWKNNM	Vaccine	murine (H-2^{k})	Dai2001
	Vaccine *Vector/Type:* recombinant protein *Strain:* 89.6 *HIV component:* gp120 *Adjuvant:* mutant R192G heat-labile toxin from E. coli as adjuvant • Promiscuous immunodominant epitopes in gp120 were mapped by overlapping peptides in CBA/J H-2^{k} and BALB/c H-2^{d} mice, and all were found to be in the outer domain, proximal to regions of structural disorder indicated by the crystal structure or by sequence divergence. • This peptide was recognized by 10/10 CBA/J with an average SI of 8.2, and not by BALB/c mice, so is considered to be uniquely immunodominant for H-2^{k} • Uniquely immunodominant sequences tended to be in the inner domain of the protein				
gp160 (81–101)	gp120 (81–101 IIIB)	PQEVVLVNVTENFNMWKND-MV?	HIV-1 infection	human	Geretti1994
	• Epitope name: B1				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 2/15 responders recognized this peptide, mean SI = 5.1.				
gp160 (92–101)	gp120 (90–100 W6.ID)	YFNMWKNNMV	Vaccine	human	Jones1999
	Vaccine *Vector/Type:* recombinant protein *Strain:* W61D *HIV component:* gp120 *Adjuvant:* QS21/MPL adjuvant • An HIV seronegative volunteer was vaccinated with rgp120 and a QS21/MPL adjuvant and HIV-1 specific T-cell lines were isolated • One T-cell clone reacts with two overlapping peptides, and the region of overlap is: YFNMWKNNMV • The first 20-mer peptide that this clone reacts with is PQEVVLGNVTEYFNMWKNNMV, and the IIIB version of this peptide does not induce proliferation in the T-cell line that responds to the W61D version: IIIB: pqevvlVnvteNfDmwknDmv.				
gp160 (92–111)	gp120 (92–111 W6.ID)	YFNMWKNNMVDQMHEDIISL	Vaccine	human	Jones1999
	Vaccine *Vector/Type:* recombinant protein *Strain:* W61D *HIV component:* gp120 *Adjuvant:* QS21/MPL adjuvant • An HIV seronegative volunteer was vaccinated with rgp120 and a QS21/MPL adjuvant and HIV-1 specific T-cell lines were isolated • The IIIB version of this peptide does not induce proliferation in the T-cell line that responds to the W61D version of the peptide NfDmwknDmvEqmhediisl. • Six T-cell lines react with this peptide, but some of these can also be stimulated by other gp120 peptides located in different regions of gp120				
gp160 (101–126)	gp120 (101–126)	VEQMHEDIISLWDQSLKPC-VKLTPLC	Vaccine	murine (H-2^k)	Sjolander1996
	Vaccine *Vector/Type:* recombinant protein *HIV component:* gp160 • Study showing that T-cell determinants from glycoproteins can be dependent on the glycosylation of the protein				
gp160 (102–114)	gp120 (109–121)	EQMHEDIISLWDQ	Vaccine	murine (H-2^{bxk})	Sastry1991
	Vaccine *Vector/Type:* peptide • Peptides induced T-cell proliferative response to immunizing peptide and to gp160				
gp160 (102–116)	gp160 (109–123 IIIB)	EQMHEDIISLWDQSL	Vaccine	murine (H-2^d, H-2^b)	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Adjuvant:* Freund's adjuvant • B10.D2 (H-$2A^d$, E^d) and B10.A(R5) (H-$2A^b$, E^b) mice immunized with rec gp160 showed a proliferative response to EQMHEDIISLWDQSL • EQMHEDIISLWDQSLKPCVK encompasses several murine Th epitopes including HEDIISLWDQSLK and is referred to as a "multideterminant region" or cluster peptide				
gp160 (102–116)	gp120 (109–123 IIIB)	EQMHEDIISLWDQSL	Vaccine	murine (H-$2^{d,i5}$)	Hale1989
	Vaccine *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 • Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types				
gp160 (102–121)	gp120 (102–121 IIIB)	EQMHEDIISLWDQSLKPCV-K?	HIV-1 infection	human	Geretti1994
	• Epitope name: B3 • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 1/15 responders recognized this peptide, SI = 5.9.				
gp160 (102–121)	gp160 (109–128 IIIB)	EQMHEDIISLWDQSLKPCVK	HIV-1 infection, Vaccine	human, murine (H-2^k, H-2^s)	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Adjuvant:* Freund's adjuvant • EQMHEDIISLWDQSLKPCVK encompasses several murine Th epitopes and is referred to as a "multideterminant region" or cluster peptide • Six multideterminant region cluster peptides were evaluated Th responses in different MHC/HLA backgrounds after vaccination of mice with gp160, or in infected people • This cluster peptide elicited proliferative responses in cells from vaccinated B10.BR mice (H-2A^k, E^k) and B10.S(9R) mice (H-2A^s, E^s), while shorter peptides from within this region stimulated H-2^k, H-2^d and H-2^b responses, but not H-2^s • IL-2 production was observed in response to this peptide in 64% (23/36) of asymptomatic HIV-infected individuals			
gp160 (105–117)	gp120 (112–124 IIIB)	HEDIISLWDQSLK	HIV-1 infection	human	Clerici1997
	• Epitope name: T2 • Used in a study of pentoxifylline's influence on HIV specific T-cells				
gp160 (105–117)	gp120 (112–124 BH10)	HEDIISLWDQSLK	Vaccine	human	Berzofsky1988
	Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* gp160 • Epitope name: T2 • Proliferative response to T1 and T2 peptides in 14 immunized, uninfected humans				
gp160 (105–117)	gp120 (112–124 IIIB)	HEDIISLWDQSLK	HIV-1 infection	human	Clerici1989
	• Epitope name: T2 • IL-2 production detection of Th lymphocytes from asymptomatic HIV-positive individuals				
gp160 (105–117)	gp120 (112–124 IIIB)	HEDIISLWDQSLK	HIV-1 infection	human	Clerici1991a
	• Epitope name: T2 • Peptides stimulate Th cell function and CTL activity in similar patient populations				
gp160 (105–117)	gp120 (112–124)	HEDIISLWDQSLK	Vaccine	human	Clerici1991b
	Vaccine *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 • Epitope name: T2 • Immunizing uninfected individuals with rgp160 results in stronger Th response than does natural infection				
gp160 (105–117)	gp120 (112–124 IIIB)	HEDIISLWDQSLK		human	Clerici1992
	• Epitope name: T2 • Cell-mediated immune response to HIV-1 peptides in HIV-1 exposed seronegative men				
gp160 (105–117)	gp120 (112–124 IIIB)	HEDIISLWDQSLK	Vaccine	Rhesus macaque	Hosmalin1991
	Vaccine *Vector/Type:* peptide prime with protein boost *Strain:* IIIB *HIV component:* gp160 • Epitope name: T2 • Peptide priming to induce T-cell help enhances antibody response to gp160 immunization				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (105–117)	gp120 (112–124 IIIB)	HEDIISLWDQSLK		human	Pinto1995
	• Epitope name: T2 • CTL activity analyzed in parallel with Th reactivity in exposed but uninfected health care workers				
gp160 (105–117)	gp120 (112–124 IIIB)	HEDIISLWDQSLK	HIV-1 infection	human	Kaul1999
	• Epitope name: T2 • Kenyan sex workers that remained seronegative were found to frequently have HIV-env peptide specific Th responses detected by an IL-2 assay (11/20 cases) and mucosal genital tract anti-HIV IgA (16/21 cases) • Helper epitopes used in this study were noted to be previously described [Clerici1989], and were not explicitly described in [Kaul1999]				
gp160 (105–117)	gp120	HEDIISLWDQSLK	HIV-1 infection, HIV-1 exposed seronegative	human	Kuhn2001
	• Epitope name: T2 • In a S. African perinatal transmission study, 33% (33/86) of cord blood samples from infants with seropositive mothers produced T-helper responses (measured by a bioassay measuring IL2 production in a murine cell line and confirmed with a proliferation assay) against a peptide cocktail containing Th epitopes P18 MN, P18 IIIB, T1, T2, and TH4 • The mothers were predominantly infected with subtype C, but the T help response was detectable in a number of cord blood samples despite using peptides based on B subtype reagents. • 3/33 infants with cord blood T help responses to Env were infected *in utero*, 2/33 were lost to follow up, and 28/33 were not infected. 6/53 of the infants with cord blood that was unresponsive to Env peptide stimulation were infected before delivery, and 8/47 contracted HIV intrapartum or via breast-feeding. • Measurable HIV specific T help responses elicited in the immunologically immature newborn, possibly in response to *in utero* exposure, are associated with a protective natural immunity that helps block mother-infant transmission of HIV-1.			
gp160 (105–117)	gp120 (112–124 IIIB)	HEDIISLWDQSLK	Vaccine	murine (H-2^k)	Hale1989
	Vaccine *Strain:* IIIB *HIV component:* gp160 • Epitope name: T2 • Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types				
gp160 (105–117)	gp160 (112–124 IIIB)	HEDIISLWDQSLK	Vaccine	murine (H-2^k)	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Adjuvant:* Freund's adjuvant • B10.BR (H-$2A^k$, E^k) mice immunized with rec gp160 showed a strong proliferative response to three overlapping peptides, QMHEDIISLWDQSL, HEDIISLWDQSLK, and DIISLWDQSLKPCVK, and HEDIISLWDQSLK is common to between them • EQMHEDIISLWDQSLKPCVK encompasses several murine Th epitopes including HEDIISLWDQSLK and is referred to as a "multideterminant region" or cluster peptide			
gp160 (105–117)	gp120 (112–124 BH10)	HEDIISLWDQSLK	computer prediction	murine (H-$2^{k,s}$)	Cease1987
	• Epitope name: T2 • 1 of 2 functional epitopes identified using an amphipathic helix epitope prediction algorithm				
gp160 (105–123)	gp120 (112–130 IIIB)	HEDIISLWDQSLKPCVKLT		human	Furci1997
	• 9/11 exposed-uninfected individuals in this study had a proliferative response to a C5 peptide, but none reacted with this previously defined epitope				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (108–119)	gp120 (108–119 LAI)	IISLWDQSLKPC	HIV-1 infection	human	Schrier1989
	• Stimulates T-cell proliferation in HIV-infected donors				
gp160 (110–125)	gp120 (110–125)	SLWDQSLKPCVKLTPL	HIV-1 infection	human	Caruso1997
	• As HIV-1-infected individuals progress to disease, T-cells show reduced ability to proliferate in response to HIV antigen, but retain the ability to express the activation antigens CD25 and CD71				
	• The ability to express activation markers in response to HIV is retained, but the response to tetanus toxoid recall antigen is lost				
	• This study investigated CD25 and CD71 expression in PBMC from patients at various stages of progression, measuring the response to in vitro stimulation by peptide cocktail containing four antigenic Env peptides, or p17 and p24				
gp160 (111–123)	gp120 (118–130)	LWDQSLKPCVKLT	Vaccine	Rhesus macaque	Nehete1993
	Vaccine *Vector/Type:* peptide				
	• Synthetic peptide derived from conserved region of the HIV-1 envelope that stimulates a proliferative response in mice				
	• Proliferative response to this peptide was observed in 3/3 immunized rhesus monkeys				
gp160 (112–130)	gp120 (112–130 IIIB)	WDQSLKPCVKLTPLCVSLK?	HIV-1 infection	human	Geretti1994
	• Epitope name: B4				
	• Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.				
	• After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.				
	• IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.				
	• 3/15 responders recognized this peptide, average SI = 4.4.				
gp160 (112–141)	gp120 (112–141 NL43)	WDQSLKPCVKLTPLCVSLK-CTDLGNATNTN	Vaccine	human	Sitz1999
	Vaccine *Vector/Type:* recombinant protein *Strain:* NL43 *HIV component:* gp120, gp160				
	• There was a great breadth of proliferative response to env peptides in 19 HIV-1 infected rgp160 and 17 HIV-1 infected rgp120 vaccine recipients				
	• Over 35% of vaccinees had a stimulation index of greater than 5 to this peptide				
gp160 (115–126)	gp120 (115–126 LAI)	SLKPCVKLTPLC	HIV-1 infection	human	Schrier1989
	• Stimulates T-cell proliferation in HIV-infected donors				
gp160 (115–129)	gp120 (115–129 LAI)	SLKPCVKLTPLCVSL	Peptide-HLA interaction	human (HLA-DR)	Gaudebout1997
	• Peptide bound to both HLA-DR*1101 and HLA-DR*0401 with high affinity				
	• Because of the distinctive binding pockets of HLA-DR*1101 and HLA-DR*0401, peptides that bound both were considered candidates for promiscuous HLA-DR binding				
gp160 (121–140)	gp120 (120–139 89.6)	KLTPLCVTLNCTNLNITKNT	Vaccine	murine	Dai2001
	Vaccine *Vector/Type:* recombinant protein *Strain:* 89.6 *HIV component:* gp120 *Adjuvant:* R192G mutant heat-labile toxin from enterotoxigenic E. coli (mLT)				
	• Epitope name: Peptide 10				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences. • This peptide was highly reactive in 5/10 BALB/c mice tested, but not in and (0/10) CBA/J mice.				
gp160 (121–141)	gp120 (131–151 IIIB)	KLTPLCVSLKCTDLKNDTN-TN?	HIV-1 infection	human	Geretti1994
	• Epitope name: C1 • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 3/15 responders recognized this peptide, average SI = 3.9.				
gp160 (122–141)	gp120 (121–140 MN)	LTPLCVTLNCTDLRNTTNTN	Vaccine	guinea pig	Chattergoon2002
	Vaccine *Vector/Type:* protein, DNA *Strain:* MN *HIV component:* gp120 *Adjuvant:* complete Freund's adjuvant (CFA) • Epitope name: 1931 • Hartley guinea pigs were intradermally injected with either recombinant protein or plasmid expressed gp120 and monitored for delayed type hypersensivity (DTH) responses after vaccination, which are related to Th1 T-cell responses. CFA did not augment responses in animals vaccinated with plasmid. • A total of 7 gp120 peptides elicited a delayed type hypersensivity (DTH) response after vaccination, out of a set of 60 overlapping peptides that spanned gp120. The vaccine delivery system, DNA versus rec protein, resulted in the recognition of distinct peptides. • 3/5 animals vaccinated with rec gp120 responded by DTH to this peptide, while 0/6 vaccinated with plasmid gp120 DNA responded.				
gp160 (122–141)	gp120 (122–141 IIIB)	LTPLCVSLKCTDLKNDTNT-N?	HIV-1 infection	human	Geretti1994
	• Epitope name: B5 • • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • 1/15 responders recognized this peptide, SI = 3.1.				
gp160 (136–155)	gp120 (141–160 MN)	NSTAWNNSNSEGTIKGGEMK	Vaccine	guinea pig	Chattergoon2002
	Vaccine *Vector/Type:* protein, DNA *Strain:* MN *HIV component:* gp120 *Adjuvant:* complete Freund's adjuvant (CFA) • Epitope name: 1932 • Hartley guinea pigs were intradermally injected with either recombinant protein or plasmid expressed gp120 and monitored for delayed type hypersensivity (DTH) responses after vaccination, which are related to Th1 T-cell responses. CFA did not augment responses in animals vaccinated with plasmid. • A total of 7 gp120 peptides elicited a delayed type hypersensivity (DTH) response after vaccination, out of a set of 60 overlapping peptides that spanned gp120. The vaccine delivery system, DNA versus rec protein, resulted in the recognition of distinct peptides. • 4/5 animals vaccinated with rec gp120 responded by DTH to this peptide, as did 2/6 vaccinated with plasmid gp120 DNA.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (138–159)	gp120 (141–160 W6.ID)	TTSNGWTGEIRKGEIKNCSF	Vaccine	human	Jones1999

Vaccine *Vector/Type:* recombinant protein *Strain:* W61D *HIV component:* gp120 *Adjuvant:* QS21/MPL adjuvant

- An HIV seronegative volunteer was vaccinated with rgp120 and a QS21/MPL adjuvant and HIV-1 specific T-cell lines were isolated
- The IIIB version of this peptide does not induce proliferation in the T-cell line that responds to the W61D version of the peptide: IIIB: ttsnSSGRMIMEgeiknesf.

gp160 (142–161)	gp120 (142–161 IIIB)	SSSGRMIMEKGEIKNCSFN-I?	HIV-1 infection	human	Geretti1994

- Epitope name: C2
- Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.
- After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.
- IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.
- Five peptides were recognized most frequently: C2 (aa 142-161), C3 (aa 152-171), C5 (aa 172-191), E5 (aa 272-291) and G4 (aa 380-393). The first three were in or near V2, the other two were proximal to the V3 and V4 loops.
- 4/15 responders recognized this immunodominant peptide, average SI = 4.3.

gp160 (147–168)	gp120 (152–173 NL43)	MMMEKGEIKNCSFNISTSI-RGK	Vaccine	human	Sitz1999

Vaccine *Vector/Type:* recombinant protein *Strain:* NL43 *HIV component:* gp120, gp160

- There was a great breadth of proliferative response to env peptides in 19 HIV-1 infected rgp160 and 17 HIV-1 infected rgp120 vaccine recipients
- Over 50% of vaccinees had a stimulation index of greater than 5 to this peptide

gp160 (152–171)	gp120 (152–171 IIIB)	GEIKNCSFNISTSIRGKVQ-K?	HIV-1 infection	human	Geretti1994

- Epitope name: C3
- Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.
- After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.
- IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.
- Five peptides were recognized most frequently: C2 (aa 142-161), C3 (aa 152-171), C5 (aa 172-191), E5 (aa 272-291) and G4 (aa 380-393). The first three were in or near V2, the other two were proximal to the V3 and V4 loops.
- 4/15 responders recognized this immunodominant peptide, average SI = 4.4.

gp160 (155–169)	Env (UG92005)	KNCSFNITTELIDKK	Vaccine	murine (H-2 IA^b)	Surman2001

Vaccine *Vector/Type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Adjuvant:* Freund's adjuvant

- This epitope is located in the V2 region of UG92005 (UG, clade D) and the hybridoma that recognized it used Vβ5
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells • Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined • Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO • 80 unique clonotypes were characterized from six mice • H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41). • Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.			
gp160 (155–169)	gp120 (160–174 LAI)	KNCSFNISTSIRGKV		human (HLA-DR)	Gaudebout1997
	• Peptide binds to both HLA-DR*1101 and HLA-DR*0401 with high affinity • Because of the distinctive binding pockets of HLA-DR*1101 and HLA-DR*0401, peptides that bound both were considered candidates for promiscuous HLA-DR binding				
gp160 (159–178)	gp120 (160–179 89.6)	FYITTSIRNKVKKEYALFNR	Vaccine	murine	Dai2001
	Vaccine *Vector/Type:* recombinant protein *Strain:* 89.6 *HIV component:* gp120 *Adjuvant:* R192G mutant heat-labile toxin from enterotoxigenic E. coli (mLT) • Epitope name: Peptide 14 • Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences. • This peptide was highly reactive in 6/10 BALB/c mice tested, and in 4/10 CBA/J mice.			
gp160 (162–181)	gp120 (162–181 IIIB)	STSIRGKVQKEYAFFYKLDI	Vaccine	Rhesus macaque	Lekutis1997b
	Vaccine *Vector/Type:* DNA *Strain:* IIIB *HIV component:* ENV • HIV-1 env DNA vaccine induced Th cell response to this epitope in a rhesus monkeys				
gp160 (162–182)	gp120 (162–182 IIIB)	STSIRGKVQKEYAFFYKLD-II?	HIV-1 infection	human	Geretti1994
	• Epitope name: C4 • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 1/15 responders recognized this peptide, SI = 3.3.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (169–189)	gp120 (141–160 W6.ID)	VQKEYALFYNLDVVPIDDD-NA	Vaccine	human	Jones1999
	Vaccine *Vector/Type:* recombinant protein *Strain:* W61D *HIV component:* gp120 *Adjuvant:* QS21/MPL adjuvant • An HIV seronegative volunteer was vaccinated with rgp120 and a QS21/MPL adjuvant and HIV-1 specific T-cell lines were isolated • The IIIB version of this peptide does not induce proliferation in the T-cell line that responds to the W61D version of the peptide ——F–K–II—N-TT vqkeyaFfyKldIIpidNdTT. • Two T-cell lines react specifically with this peptide				
gp160 (172–191)	gp120 (172–191 IIIB)	EYAFFYKLDIIPIDNDTTSY	Vaccine	Rhesus macaque	Lekutis1997b
	Vaccine *Vector/Type:* DNA *Strain:* IIIB *HIV component:* ENV • HIV-1 env DNA vaccine induced Th cell response to this epitope in a rhesus monkey				
gp160 (172–191)	gp120 (172–191 IIIB)	EYAFFYKLDIIPIDNDTTS-Y?	HIV-1 infection	human	Geretti1994
	• Epitope name: C5 • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • Five peptides were recognized most frequently: C2 (aa 142-161), C3 (aa 152-171), C5 (aa 172-191), E5 (aa 272-291) and G4 (aa 380-393). The first three were in or near V2, the other two were proximal to the V3 and V4 loops. • 4/15 responders recognized this immunodominant peptide, average SI = 7.4.				
gp160 (175–189)	Env (UG92005)	LFYKLDVVQIDNSTN	Vaccine	murine (H-2 IA^b)	Surman2001
	Vaccine *Vector/Type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Adjuvant:* Freund's adjuvant • This epitope is located in the V2 region of UG92005 (UG, clade D) and the Vβ usage of the TCR was not determined • C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant • The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells • Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined • Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO • 80 unique clonotypes were characterized from six mice • H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41).			

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.				
gp160 (186–215)	gp120 (191–220 NL43)	NDTTSYTLTSCNTSVITQA-CPKVSFEPIPI	Vaccine	human	Sitz1999
	Vaccine *Vector/Type:* recombinant protein *Strain:* NL43 *HIV component:* gp120, gp160 • There was a great breadth of proliferative response to env peptides in 19 HIV-1 infected rgp160 and 17 HIV-1 infected rgp120 vaccine recipients • Over 30% of vaccinees had a stimulation index of greater than 5 to this peptide				
gp160 (188–207)	gp120 (89.6)	NTKYRLISCNTSVITQACPK	Vaccine	murine	Dai2001
	Vaccine *Vector/Type:* recombinant protein *Strain:* 89.6 *HIV component:* gp120 *Adjuvant:* R192G mutant heat-labile toxin from enterotoxigenic E. coli (mLT) • Epitope name: Peptide 17 • Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences. • This peptide was reactive in only 1/10 BALB/c mice tested, but was one of the most reactive in CBA/J mice, reacting with 9/10 mice.				
gp160 (188–207)	gp120 (190–209 89.6)	NTKYRLISCNTSVITQACPK	Vaccine	murine (H-2^k)	Dai2001
	Vaccine *Vector/Type:* recombinant protein *Strain:* 89.6 *HIV component:* gp120 *Adjuvant:* mutant R192G heat-labile toxin from E. coli as adjuvant • Promiscuous immunodominant epitopes in gp120 were mapped by overlapping peptides in CBA/J H-2^k and BALB/c H-2^d mice, and all were found to be in the outer domain, proximal to regions of structural disorder indicated by the crystal structure or by sequence divergence. • This peptide was recognized by 9/10 CBA/J with an average SI of 9.8, one of the two immunodominant peptides in CBA/J mice, and not by BALB/c mice, so is considered to be uniquely immunodominant for H-2^k • Uniquely immunodominant sequences tended to be in the inner domain of the protein				
gp160 (192–211)	gp120 (192–211 IIIB)	KLTSCNTSVITQACPKVSF-E?	HIV-1 infection	human	Geretti1994
	• Epitope name: D2 • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 1/15 responders recognized this peptide, SI = 3.6.				
gp160 (193–218)	gp120 (193–218)	LTSCNSVITQACPKVSFEP-IPIHYC	Vaccine	murine (H-$2^{d,b}$)	Sjolander1996
	Vaccine *Vector/Type:* recombinant protein *HIV component:* gp160 • Study showing that T-cell determinants from glycoproteins can be dependent on the glycosylation of the protein				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (198–212)	Env (1007)	TSVITQACPKVSFEP	Vaccine	murine (H-2 IA^b)	Surman2001

Vaccine *Vector/Type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Adjuvant:* Freund's adjuvant

- This epitope is located in the C2 region of 1007 (US, clade B) and the Vβ usage of the TCRs for two clonotypes was Vβ3 and Vβ8.1-2
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO
- 80 unique clonotypes were characterized from six mice
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41).
- Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.

gp160 (198–215)	Env (1007)	TSVITQACPKVSFEPIPI	Vaccine	murine (H-2 IA^b)	Surman2001

Vaccine *Vector/Type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Adjuvant:* Freund's adjuvant

- This epitope is located in the C2 region of 1007 (US, clade B) and the Vβ usage of the TCR was Vβ6
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO
- 80 unique clonotypes were characterized from six mice
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41).
- Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.

gp160 (199–211)	Env (204–216)	SVITQACSKVSFE	Vaccine	Rhesus macaque	Nehete1993

Vaccine *Vector/Type:* peptide

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Synthetic peptide derived from conserved region of the HIV-1 envelope that stimulates a proliferative response in mice • A weak or transient proliferative response to this peptide was observed in 3/3 immunized rhesus monkeys				
gp160 (199–211)	Env (204–216)	SVITQACSKVSFE	HIV-1 infection	human, chimpanzee	Nehete1998b
	• HIV-infected chimpanzees and HIV-positive patients show positive proliferative responses to multiple peptides from five conserved regions of the HIV-1 Env				
gp160 (199–211)	gp120 (204–216) **Vaccine** *Vector/Type:* peptide	SVITQACSKVSFE	Vaccine	murine (H-$2^{bxk,sxd}$)	Sastry1991
	• Peptides induced T-cell proliferative response in mice representing four haplotypes				
gp160 (200–214)	gp120 (205–219 LAI)	VITQACPKVSFEPIP	Peptide-HLA interaction	human (HLA-DR)	Gaudebout1997
	• Peptide binds to both HLA-DR*1101 and HLA-DR*0401 with high affinity • Because of the distinctive binding pockets of HLA-DR*1101 and HLA-DR*0401, peptides that bound both were considered candidates for promiscuous HLA-DR binding				
gp160 (201–212)	Env (1007)	ITQACPKVSFEP	Vaccine	murine (H-2 IA^b)	Surman2001
	Vaccine *Vector/Type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Adjuvant:* Freund's adjuvant • This epitope is located in the C2 region of 1007 (US, clade B) and the Vβ usage of the TCR was Vβ3 • The epitope described here is the region of overlap of two 15 mers that were both able to stimulate IL-2 production from the hybridoma (TSVITQACPKVSFEP and ITQACPKVSFEPIPI) • C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant • The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells • Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined • Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO • 80 unique clonotypes were characterized from six mice • H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41). • Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.				
gp160 (206–220)	Env (1007)	PKVSFEPIPIHYCAP	Vaccine	murine (H-2 IA^b)	Surman2001
	Vaccine *Vector/Type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Adjuvant:* Freund's adjuvant • This epitope is located in the C2 region of 1007 (US, clade B) and 12 hybridomas recognized the peptide with Vβ usage of Vβ4,6,7,8.1-2,8.3,11,12 and others not determined				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant • The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells • Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined • Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO • 80 unique clonotypes were characterized from six mice • H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41). • Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.				
gp160 (206–225)	gp120 (211–230 MN)	PKISFEPIPIHYCAPAGFAI	Vaccine	guinea pig	Chattergoon2002
	Vaccine *Vector/Type:* protein, DNA *Strain:* MN *HIV component:* gp120 *Adjuvant:* complete Freund's adjuvant (CFA) • Epitope name: 1957 • Hartley guinea pigs were intradermally injected with either recombinant protein or plasmid expressed gp120 and monitored for delayed type hypersensivity (DTH) responses after vaccination, which are related to Th1 T-cell responses. CFA did not augment responses in animals vaccinated with plasmid. • A total of 7 gp120 peptides elicited a delayed type hypersensivity (DTH) response after vaccination, out of a set of 60 overlapping peptides that spanned gp120. The vaccine delivery system, DNA versus rec protein, resulted in the recognition of distinct peptides. • 5/5 animals vaccinated with rec gp120 responded by DTH to this peptide, as did 2/6 vaccinated with plasmid gp120 DNA.				
gp160 (206–230)	gp120 (206–230)	PKVSFEPIPIHYCAPAGFA-ILKCNN	Vaccine	murine (H-$2^{d,b}$)	Sjolander1996
	Vaccine *Vector/Type:* recombinant protein *HIV component:* gp160 • Study showing that T-cell determinants from glycoproteins can be dependent on the glycosylation of the protein				
gp160 (208–218)	Env (UG92005)	ITFEPIPIHYC	Vaccine	murine (H-2 IA^b)	Surman2001
	Vaccine *Vector/Type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Adjuvant:* Freund's adjuvant • This epitope is located in the C2 region of UG92005 (UG, clade D) and its was recognized by two hybridomas with Vβ usage Vβ12 and not determined • The epitope described here is the region of overlap of two 15 mers that were both able to stimulate IL-2 production from the hybridoma (PKITFEPIPIHYCAP and ITFEPIPIHYCAPAG) • C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant • The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells • Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO • 80 unique clonotypes were characterized from six mice • H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41). • Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.				
gp160 (208–222)	Env (UG92005)	ITFEPIPIHYCAPAG	Vaccine	murine (H-2 IA^b)	Surman2001
	Vaccine *Vector/Type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Adjuvant:* Freund's adjuvant • This epitope is located in the C2 region of UG92005 (UG, clade D) and it was recognized by five hybridomas with Vβ usage Vβ5, 8.2, 12 and not determined • C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant • The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells • Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined • Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO • 80 unique clonotypes were characterized from six mice • H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41). • Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.				
gp160 (208–227)	gp120 (210–229 89.6)	VSFQPIPIHYCVPAGFAMLK	Vaccine	murine	Dai2001
	Vaccine *Vector/Type:* recombinant protein *Strain:* 89.6 *HIV component:* gp120 *Adjuvant:* R192G mutant heat-labile toxin from enterotoxigenic E. coli (mLT) • Epitope name: Peptide 19 • Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences. • This peptide was reactive in 6/10 BALB/c mice tested, and in 6/10 CBA/J mice.				
gp160 (210–223)	gp120 (215–228)	FEPIPIHYCAFPGF	Vaccine	murine (H-2^{bxk})	Sastry1991
	Vaccine *Vector/Type:* peptide				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Peptides induced T-cell proliferative response to immunizing peptide and to gp160				
gp160 (212–231)	gp120 (221–240 W6.ID)	PIPIHYCAPAGFAILKCNNK	Vaccine	human	Jones1999
	Vaccine *Vector/Type:* recombinant protein *Strain:* W61D *HIV component:* gp120 *Adjuvant:* QS21/MPL adjuvant • An HIV seronegative volunteer was vaccinated with rgp120 and a QS21/MPL adjuvant and HIV-1 specific T-cell lines were isolated • Two T-cell lines react specifically with this peptide				
gp160 (212–231)	gp120 (212–231 IIIB)	PIPIHYCAPAGFAILKCNN-K?	HIV-1 infection	human	Geretti1994
	• Epitope name: D4 • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 3/15 responders recognized this peptide, average SI = 4.2.				
gp160 (214–220)	Env (1007)	PIHYCAP	Vaccine	murine (H-2 IA^b)	Surman2001
	Vaccine *Vector/Type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Adjuvant:* Freund's adjuvant • This epitope is located in the C2 region of 1007 (US, clade B) and the Vβ usage of the TCR was not determined • The epitope described here is the region of overlap of two 15 mers that were both able to stimulate IL-2 production from the hybridoma (PKVSFEPIPIHYCAP and PIHYCAPAGFAILKC) • C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant • The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells • Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined • Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO • 80 unique clonotypes were characterized from six mice • H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41). • Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.				
gp160 (215–225)	Env (1007)	IHYCAPAGFAI	Vaccine	murine (H-2 IA^b)	Surman2001
	Vaccine *Vector/Type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Adjuvant:* Freund's adjuvant • This epitope is located in the C2 region of 1007 (US, clade B) and the Vβ usage of the TCR was not determined				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The epitope described here is the region of overlap of two 15 mers that were both able to stimulate IL-2 production from the hybridoma (EPIPIHYCAPAGFAI and IHYCAPAGFAILKCN) • C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant • The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells • Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined • Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO • 80 unique clonotypes were characterized from six mice • H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41). • Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.			
gp160 (216–225)	Env (UG92005)	HYCAPAGFAI	Vaccine	murine (H-2 IA^b)	Surman2001
	Vaccine *Vector/Type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Adjuvant:* Freund's adjuvant • This epitope is located in the C2 region of UG92005 (UG, clade D) and Vβ usage of its TCR was not determined • The epitope described here is the region of overlap of two 15 mers that were both able to stimulate IL-2 production from the hybridoma (EPIPIHYCAPAGFAI and HYCAPAGFAILKCND) • C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant • The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells • Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined • Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO • 80 unique clonotypes were characterized from six mice • H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41). • Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.			
gp160 (220–234)	gp120 (225–240 SF2)	PAGFAILKCNNKTFN	in vitro stimulation		Manca1993
	• T-cell line derived from unprimed, uninfected individual				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Responds to APC pulsed with either synthetic peptide or gp120 • Human MAbs 448-D and 450-D enhance APC gp120 uptake and presentation				
gp160 (220–234)	gp120 (IIIB)	PAGFAILKCNNKTFN	Vaccine	human	Pozzi1994
	Vaccine *Vector/Type:* Streptococcus gordonii *HIV component:* gp120 • Epitope name: pep24 • This previously described immunodominant Th cell epitope was fused to the streptococcal surface protein M6 (emm-6.1), for expression on the surface of the bacterium Streptococcus gordonii. • Recombinant bacteria showed efficient MHC class II mediated presentation of gp120 to T-cells by stimulation of a proliferative response in a human T cell clone specific for pep24.				
gp160 (220–235)	gp120 (IIIB)	PAGFAILKCNNKTFNY	in vitro stimulation	human (DR2)	Manca1995b
	• Peptide stimulation of PBMC from non-infected individuals in vitro • Peptide priming does not always induce T-cells that recognize whole protein • gp120 priming induced T-cells that recognize this peptide				
gp160 (220–235)	gp120 (220–235 HXB2)	PAGFAILKCNNKTFNY	in vitro stimulation	human (DR2)	Guzman1998
	• Listeria monocytogenes, an intracellular pathogen which is ingested by macrophages and can escape from the phagosome to replicate in the cytoplasm, was used successfully as carrier to deliver this gp120 epitope to CD4+ T-cells				
gp160 (220–235)	gp120 (191–205 HXB2)	PAGFAILKCNNKTFNY	in vitro stimulation	human (DR2)	Fenoglio1999
	• gp120 pep24 epitope exhibited antagonistic activity against proliferation of gp120-specific T-cells when flanked by unrelated amino acid sequence • The glutathione S-transferase (GST)-peptide system can be used to display peptides; antigenicity was maintained when this peptide was expressed at the C-term end, but antagonism resulted when this peptide was expressed at the N-term end				
gp160 (222–241)	gp120 (222–241 IIIB)	GFAILKCNNKTFNGTGPCT-N?	HIV-1 infection	human	Geretti1994
	• Epitope name: D5 • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 2/15 responders recognized this peptide, average SI = 4.8.				
gp160 (223–231)	gp120 (238–246 HXB2)	FAILKCNNK	in vitro stimulation	human	Li Pira1998
	• Clonal heterogeneity was broad for a recall response to tetanus toxoid or PPD, but oligoclonal to primary HIV antigens, dominated in this case by TCR Vβ 22 usage • Donor of PBMC that recognized this epitope had HLA-DR alleles 2 and 6 • The only (detected) immunogenic variant of this epitope was derived from strain NOF (YAILKCNNK)				
gp160 (223–231)	gp120 (194–202 HXB2)	FAILKCNNK	in vitro stimulation	human (DR2, 6)	Manca1996
	• Epitope was the minimal stimulatory sequence defined for two Th lines stimulated in vitro • One Th line was stimulated by gp120, one by a Glutathione-S-transferase (GST)-peptide fusion • Alanine substitutions at position 914, 196, and 202 abrogated activity for the GST-peptide stimulated line, but not for a gp120 stimulated line				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Constructs combining GST and the PAGFAILKCNNKTFNY gp120 peptide at the C-term end of GST stimulated Th cells but not at the N-term end				
gp160 (223–231)	gp120 (194–202 HXB2)	FAILKCNNK	in vitro stimulation	human (DR2, 6)	Manca1996
	• Epitope was the minimal stimulatory sequence defined for two Th lines stimulated in vitro • One Th line was stimulated by p66, one by a Glutathione-S-transferase (GST)-peptide fusion protein • Alanine substitutions at position 914, 196, and 202 abrogated activity for the GST-peptide stimulated line, but not for a gp120 stimulated line • Constructs linking GST to the PAGFAILKCNNKTFNY gp120 peptide at the C-term end of GST stimulated Th cells, constructs linking at the N-term end did not • The C and N termini of GST are not intrinsically permissive or non-permissive, presentation is epitope specific (see SSTVNDIQKLV for contrast)				
gp160 (223–231)	gp120 (237–245 SF2, HXB2)	FAILKCNNK		murine BALB/c (H-2^d)	Fenoglio2000
	• This peptide is an immunodominant Th epitope in BALB/c mice • Substitutions in positions 237, 241, 243, 244 with Ala all cause reduced recognition • Most natural analogs they tested did not cross-react, including peptides based on clade A, B, C, D, E and O sequences • Position 237 and 244 when substituted with Ala cause an antagonistic response and the natural analogues of this epitope to loose antigenicity • Some of the naturally occurring variants also cause an antagonistic response				
gp160 (230–245)	gp120 (IIIB)	NKTFNGKGPCTNVSTY	in vitro stimulation	human	Manca1995b
	• Peptide stimulation of PBMC from non-infected individuals in vitro • Peptide priming does not always induce T-cells that recognize whole protein				
gp160 (232–251)	gp120 (232–251 IIIB)	TFNGTGPCTNVSTVQCTHG-I?	HIV-1 infection	human	Geretti1994
	• Epitope name: E1 • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 3/15 responders recognized this peptide, average SI = 3.9.				
gp160 (235–247)	gp120 (240–252)	GTGPCTNVSTVQC	Vaccine	Rhesus macaque	Nehete1993
	Vaccine *Vector/Type:* peptide • Synthetic peptide derived from conserved region of the HIV-1 envelope that stimulates a proliferative response in mice • Proliferative response to this peptide was observed in 1/3 immunized rhesus monkeys, with a weak transient response in the other two				
gp160 (238–257)	gp120 (240–249 89.6)	PCTNVSTVQCTHGIRPVVST	Vaccine	murine	Dai2001
	Vaccine *Vector/Type:* recombinant protein *Strain:* 89.6 *HIV component:* gp120 *Adjuvant:* R192G mutant heat-labile toxin from enterotoxigenic E. coli (mLT) • Epitope name: Peptide 22 • Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This peptide was highly reactive in 6/10 BALB/c mice tested, but not in any (0/10) CBA/J mice.				
gp160 (240–255)	gp120 (IIIB) • Peptide stimulation of PBMC from non-infected individuals in vitro	TNVSTVQCTHGRPIY	in vitro stimulation	human	Manca1995b
gp160 (242–261)	gp120 (242–261 IIIB) • Epitope name: E2 • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 1/15 responders recognized this peptide, SI = 3.4.	VSTVQCTHGIRPVVSTQLL-L?	HIV-1 infection	human	Geretti1994
gp160 (242–261)	gp120 (242–261 IIIB) • A novel C2 region Th epitope was described in SHIV-89.6 infected Macaca mulatta	VSTVQCTHGIRPVVSTQLLL	SHIV infection	Rhesus macaque (DRB1*0406)	Lekutis1997a
gp160 (250–265)	gp120 (IIIB) • Peptide stimulation of PBMC from non-infected individuals in vitro • Peptide priming does not always induce T-cells that recognize whole protein	GIRPIVSTQLLLNGSC	in vitro stimulation	human	Manca1995b
gp160 (252–271)	gp120 (252–271 IIIB) • Epitope name: E3 • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 1/15 responders recognized this peptide, average SI = 7.4.	RPVVSTQLLLNGSLAEEEV-V?	HIV-1 infection	human	Geretti1994
gp160 (262–281)	gp120 (262–281 IIIB) • Epitope name: E4 • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 2/15 responders recognized this peptide, average SI = 3.1.	NGSLAEEEVVIRSVNFTDN-A?	HIV-1 infection	human	Geretti1994

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (264–287)	gp120 (269–292 NL43)	SLAEEEVVIRSANFTDNAK-TIIVQ	Vaccine	human	Sitz1999
	Vaccine *Vector/Type:* recombinant protein *Strain:* NL43 *HIV component:* gp120, gp160 • There was a great breadth of proliferative response to env peptides in 19 HIV-1 infected rgp160 and 17 HIV-1 infected rgp120 vaccine recipients • 50% of vaccinees had a stimulation index of greater than 5 to this peptide				
gp160 (269–283)	gp120 (269–283 IIIB, B10)	EVVIRSANFTDNAKT	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				
gp160 (270–285)	gp120 (IIIB)	VVIRSDNFTNNAKTIC	in vitro stimulation	human	Manca1995b
	• Peptide stimulation of PBMC from non-infected individuals in vitro • Peptide priming does not always induce T-cells that recognize whole protein				
gp160 (272–291)	gp120 (272–291 IIIB)	IRSVNFTDNAKTIIVQLNT-S?	HIV-1 infection	human	Geretti1994
	• Epitope name: E5 • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • Five peptides were recognized most frequently: C2 (aa 142-161), C3 (aa 152-171), C5 (aa 172-191), E5 (aa 272-291) and G4 (aa 380-393). The first three were in or near V2, the other two were proximal to the V3 and V4 loops. • 4/15 responders recognized this immunodominant peptide, average SI = 5.0.				
gp160 (274–288)	gp120 (274–288 IIIB, B10)	SANFTDNAKTIIVQL	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				
gp160 (280–296)	gp120 (IIIB)	NAKTIIVQLNESVAIC	in vitro stimulation	human	Manca1995b
	• Peptide stimulation of PBMC from non-infected individuals in vitro • Peptide priming does not always induce T-cells that recognize whole protein				
gp160 (288–307)	gp120 (290–309 89.6)	LNESVVINCTRPNNNTRRRL	Vaccine	murine	Dai2001
	Vaccine *Vector/Type:* recombinant protein *Strain:* 89.6 *HIV component:* gp120 *Adjuvant:* R192G mutant heat-labile toxin from enterotoxigenic E. coli (mLT) • Epitope name: Peptide 27 • Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences. • This peptide was reactive in only 1/10 BALB/c mice tested, but reacted in 8/10 CBA/J mice.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (289–297)	gp120 (292–300 SF2)	NESVAINCT	Vaccine	human	Botarelli1991
	Vaccine *Vector/Type:* recombinant protein *Strain:* SF2 *HIV component:* gp120				
	• A non-glycosylated form of SF2 gp120, env 2-3, was used as an immunogen – 20% of T-cell clones do not recognize the glycosylated form				
gp160 (290–306)	gp120 (296–312 LAI)	SVVEINCTRPNNNTRKS	HIV-1 infection	human	Schrier1989
	• Stimulates T-cell proliferation in HIV-infected donors				
gp160 (292–310)	gp120 (292–310 IIIB)	VEINCTRPNNNTRKRIRIQ?	HIV-1 infection	human	Geretti1994
	• Epitope name: F1				
	• Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.				
	• After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.				
	• IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.				
	• Only 1/15 responders recognized this peptide, but it had the highest SI in the study of 9.9.				
gp160 (296–307)	gp120 (301–324 RF)	CTRPNNNTRKSI	HIV-1 infection		deLorimier1994
	• Proton NMR spectroscopy was employed to analyze the solution conformation of a hybrid peptide, T1-SP10RF, in order to better understand the immunogenicity of its' T helper (KQIINMWQEVGKAMYA, CTRPNNNTRKSI), CTL (SITKGPGRVIYATG) and B-cell epitopes (RKSITKGPGRVIYATG).				
	• This epitope embedded in the T1-SP10RF peptide does not form a helical amphipathic conformation. It lacks random-coil conformations, and this may make a peptide less susceptible to complete proteolytic degredation and be favored within epitopes.				
gp160 (296–314)	gp120 (303–321 IIIB)	CTRPNNNTRKSIRIQRGPG-(Y)	Vaccine	goat	Palker1989
	Vaccine *Vector/Type:* peptide *Strain:* IIIB				
	• Goats were immunized with peptides containing V3 type-specific neutralizing determinants coupled to T1				
gp160 (297–321)	gp120 (302–324 MN)	TRPNYNKRKRIHIGPGRAF-YTTK	Vaccine	murine BALB/c (H-2^d)	Oscherwitz1999b
	Vaccine *Vector/Type:* peptide *Strain:* MN *HIV component:* V3				
	• Epitope presented as a tandem repeat (eight copies) elicits stronger B-cell and T-cell responses than the epitope presented as a single copy				
	• This study indicates that the increased response was not due to neodeterminants created at the junction of the peptides, but rather due to an epitope density effect, increased immunogenicity through a high ratio of epitope to protein				
gp160 (297–330)	Env (303–335 BX08)	TRPNNNTRKSIHIGPGRAF-YATGEIIGDIRQAH	Vaccine	human	Gahery-Segard2000
	Vaccine *Vector/Type:* lipopeptide				
	• Anti-HIV lipopeptide vaccine consisting of six long peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial				
	• A CD4+ T cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 6/10 reacted to this peptide				
	• 9/12 tested mounted a CTL responses to at least one of the six peptides, each of the six peptides elicited a CTL response in at least one individual – this peptide was particularly immunogenic, eliciting a CTL response in five vaccinees				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• None of the 12 tested had an IgG response to gp120 or gp160 and vaccinees could be differentiated from HIV-1 seropositive individuals with a commercial HIV detection kit – no neutralizing antibodies were observed				
gp160 (298–307)	Env (UG92005)	RPYNNTRKGI	Vaccine	murine (H-2 IA^b)	Surman2001
	Vaccine *Vector/Type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Adjuvant:* Freund's adjuvant				
	• This epitope is located in the V3 region of UG92005 (UG, clade D) and was recognized by a hybridoma with Vβ usage not determined				
	• The epitope described here is the region of overlap of two 15 mers that were both able to stimulate IL-2 production from the hybridoma (TINCTRPYNNTRKGI and RPYNNTRKGIHIGPG)				
	• C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant				
	• The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells				
	• Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined				
	• Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO				
	• 80 unique clonotypes were characterized from six mice				
	• H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41).				
	• Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.				
gp160 (298–319)	gp120 (300–319 89.6)	RPNNNTRRRLSIGPGRAFYA	Vaccine	murine	Dai2001
	Vaccine *Vector/Type:* recombinant protein *Strain:* 89.6 *HIV component:* gp120 *Adjuvant:* R192G mutant heat-labile toxin from enterotoxigenic E. coli (mLT)				
	• Epitope name: Peptide 28				
	• Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences.				
	• This peptide was reactive in 7/10 BALB/c mice tested, and in 5/10 CBA/J mice.				
gp160 (301–325)	gp120 (IIIB)	NNTRKSIRIQRGPGRAFVT-IGKIGN	Vaccine	murine	Sasaki1998
	Vaccine *Vector/Type:* DNA *Strain:* IIIB *HIV component:* ENV, REV *Adjuvant:* QS-21 adjuvant				
	• The env response is what is being sought, but co-expression of rev is required				
	• Intramuscular versus nasal vaccination with DNA vaccine with a QS-21 adjuvant was studied				
	• QS-21 enhanced the IgG2a response mediated via Th1 cytokines IFNγ and IL-2 and delayed type hypersensitivity (DTH) in response to the V3 peptide was measured by a foot pad swelling test [Sasaki1998]				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (302–315)	gp120 (307–322 IIIB)	NTRKSIRIQRGPGR	Vaccine	murine	Goodman-Snitkoff1990
	Vaccine *Vector/Type:* peptide *Strain:* IIIB *HIV component:* V3				
	• Identification of putative Th epitopes that can stimulate an antibody response in peptide-immunized mice				
gp160 (302–321)	gp120 (302–321 IIIB)	NTRKRIRIQRGPGRAFVTI-G?	HIV-1 infection	human	Geretti1994
	• Epitope name: F2				
	• Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.				
	• After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.				
	• IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.				
	• 1/15 responders recognized this peptide, SI = 5.6.				
gp160 (302–327)	gp120 (307–332 MN)	NKRKRIHIGPGRAFYTTKN-IIGTIR	Vaccine	murine	Anderson2001
	Vaccine *Vector/Type:* peptide *Strain:* MN *HIV component:* V3 *Adjuvant:* Montainde ISA-51				
	• Hypervariable epitope constructs (HECs) are degenerative peptide cocktails that are made in a single peptide synthesis reaction. Vaccination with a V3 degenerative peptide cocktail containing 64 distinct peptides, NTRK-[SR]-I-[HR]-IGPG-[RQ]-AFY-[AT]-TG-[DE]-IG-[DN]-IRQ, elicited broader and more durable Th responses than the MN V3 peptide alone in BALB/c mice immunized and boosted with V3 peptides, although the MN peptide elicited a transient MN-specific V3 response.				
gp160 (305–321)	gp120 (312–329)	(CG)KSIRIQRGPGRAFVT-IG	HIV-1 infection	human	Adams1997
	• Used as positive control in study examining T-cell response to four p24 Gag peptides				
gp160 (308–319)	gp120 (subtype C)	(CKR)KIHIGPGQAFYT	HIV-1 infection	murine (H-$2^{b,d,k,s}$)	Ahluwalia1997
	• A V3 loop peptide modified to resemble an Indian form (GPGQ) was incorporated into ISCOMS (immune stimulating complexes) or liposomes, and used to immunize mice – the IgG2a/IgG2b Ab response was enhanced by the presentation in the ISCOM suggestive of a Th1 response				
gp160 (308–321)	gp120 (MN)	RIHIGPGRAFYTTK	Vaccine	murine (H-2^{d})	Klinman1995
	Vaccine *Vector/Type:* peptide *Strain:* MN *HIV component:* V3				
	• Epitope name: SP10				
	• Hybrid T1-V3 peptide activates IL-4 and IL-6 in a dose dependent manner				
	• 10-mer from V3 contributes to this response				
gp160 (308–322)	gp120 (308–322 IIIB)	RIHIGPGRAFYTTKN		human	Furci1997
	• 9/11 exposed-uninfected individuals in this study had a proliferative response to a C5 peptide, but only 1/11 exposed-uninfected individuals recognized this peptide				
	• 1/18 unexposed-uninfected controls could recognize this peptide				
	• Erroneously documented as IIIB sequence - most likely MN peptide				
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK	Vaccine	Rhesus macaque	Nehete1993
	Vaccine *Vector/Type:* peptide				
	• Epitope name: P18				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Synthetic peptide derived from conserved region of the HIV-1 envelope that stimulates a proliferative response in mice • Despite the proliferative response to this peptide in mice and humans, no response was observed in 3 rhesus monkeys				
gp160 (308–322)	gp120 (315–329 IIIB) • Epitope name: P18 • The breadth and intensity of the CTL response and the type of Th response was studied in seven rapidly progressing HIV-1+ infants • IL-2 and γ IFN production from Th1 cells correlated with the CTLp frequency against HIV-1 Gag, Env, Nef and Pol • IL-4 production from Th2 cells was inversely correlated with the CTLp frequency • The HIV-1+ children with strong CTL responses had levels of anti-CD3 MAb induction of Th1 cells comparable to uninfected children • The children that did not mount a good CTL response had dramatically decreased numbers of Th1 relative to Th2 cells	RIQRGPGRAFVTIGK	HIV-1 infection	human	Wasik1997
gp160 (308–322)	gp120 (315–329 IIIB) • Epitope name: P18 • Th responses measured by IL-2 responses to P18 and T1 in HIV-1 infected infants were undetectable at less than 1 month of age, and remained low in children with AIDS symptoms, but increased with age in children with slowly progressive disease • The kinetics and intensity of the CTL activity during the first year of life was related to the child's ability to make Th1 responses	RIQRGPGRAFVTIGK	HIV-1 infection	human	Wasik2000
gp160 (308–322)	gp120 (315–329 IIIB) • Epitope name: P18 • CTL activity analyzed in parallel with Th reactivity in exposed but uninfected health care workers	RIQRGPGRAFVTIGK		human	Pinto1995
gp160 (308–322)	gp120 (315–329 MN) • Epitope name: P18 • CTL activity analyzed in parallel with Th reactivity in exposed but uninfected health care workers	RIHIGPGRAFYTTKN		human	Pinto1995
gp160 (308–322)	gp120 (315–329 IIIB) • Epitope name: P18 • IL-2 production detection of Th lymphocytes from asymptomatic HIV-positive individuals	RIQRGPGRAFVTIGK	HIV-1 infection	human	Clerici1989
gp160 (308–322)	gp120 (315–329 IIIB) • Epitope name: P18 • Peptides stimulate Th cell function and CTL activity in similar patient populations	RIQRGPGRAFVTIGK	HIV-1 infection	human	Clerici1991a
gp160 (308–322)	gp120 (315–329 IIIB) **Vaccine** *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 • Epitope name: P18 • Immunizing uninfected individuals with rgp160 results in stronger Th response than does natural infection	RIQRGPGRAFVTIGK	Vaccine	human	Clerici1991b
gp160 (308–322)	gp120 (315–329 IIIB) • Epitope name: P18 • Cell-mediated immune response to HIV-1 peptides in HIV-1 exposed seronegative men	RIQRGPGRAFVTIGK		human	Clerici1992
gp160 (308–322)	gp120 (315–329 IIIB) • Epitope name: P18 • used in a study of the influence of pentoxifylline on HIV specific T-cells	RIQRGPGRAFVTIGK	HIV-1 infection	human	Clerici1997

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (308–322)	gp120 (MN)	RIHIGPGRAFYTTKN		human	Clerici1992
	• Epitope P18 MN: Cell-mediated immune response to HIV-1 peptides in HIV-1 exposed seronegative men				
gp160 (308–322)	gp160 (315–329 IIIB)	RIQRGPGRAFVTIGK	HIV-1 infection, HIV-1 exposed seronegative	human	Wasik1999
	• Epitope name: P18 • IL-2 responses associated with beta-chemokine expression were detectable at birth in the majority of uninfected infants born to HIV+ mothers, declining by age 6 months • In both uninfected and infected infants of HIV-positive mothers, responses to the T1 peptide (KQIINMWQEVGKAMYA) were more frequent than responses to P18 • T1 is a highly conserved epitope, whereas P18 has a higher mutation rate due to its location in the immunodominant V3 loop region				
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK	HIV-1 infection	human	Kaul1999
	• Epitope name: P18 • Kenyan sex workers that remained seronegative were found to frequently have HIV-env peptide specific Th responses detected by an IL-2 assay (11/20 cases) and mucosal genital tract anti-HIV IgA (16/21 cases) • Helper epitopes used in this study were noted to be previously described [Clerici1989], and were not explicitly described in [Kaul1999]				
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK	HIV-1 infection, HIV-1 exposed seronegative	human	Kuhn2001
	• Epitope name: P18 • In a S. African perinatal transmission study, 33% (33/86) of cord blood samples from infants with seropositive mothers produced T-helper responses (measured by a bioassay measuring IL2 production in a murine cell line and confirmed with a proliferation assay) against a peptide cocktail containing Th epitopes P18 MN, P18 IIIB, T1, T2, and TH4 • The mothers were predominantly infected with subtype C, but the T help response was detectable in a number of cord blood samples despite using peptides based on B subtype reagents. • 3/33 infants with cord blood T help responses to Env were infected *in utero*, 2/33 were lost to follow up, and 28/33 were not infected. 6/53 of the infants with cord blood that was unresponsive to Env peptide stimulation were infected before delivery, and 8/47 contracted HIV intrapartum or via breast-feeding. • Measurable HIV specific T help responses elicited in the immunologically immature newborn, possibly in response to *in utero* exposure, are associated with a protective natural immunity that helps block mother-infant transmission of HIV-1.				
gp160 (308–322)	gp120 (315–329 MN)	RIHIGPGRAFYTTKN	HIV-1 infection, HIV-1 exposed seronegative	human	Kuhn2001
	• Epitope name: P18 • In a S. African perinatal transmission study, 33% (33/86) of cord blood samples from infants with seropositive mothers produced T-helper responses (measured by a bioassay measuring IL2 production in a murine cell line and confirmed with a proliferation assay) against a peptide cocktail containing Th epitopes P18 MN, P18 IIIB, T1, T2, and TH4 • The mothers were predominantly infected with subtype C, but the T help response was detectable in a number of cord blood samples despite using peptides based on B subtype reagents. • 3/33 infants with cord blood T help responses to Env were infected *in utero*, 2/33 were lost to follow up, and 28/33 were not infected. 6/53 of the infants with cord blood that was unresponsive to Env peptide stimulation were infected before delivery, and 8/47 contracted HIV intrapartum or via breast-feeding. • Measurable HIV specific T help responses elicited in the immunologically immature newborn, possibly in response to *in utero* exposure, are associated with a protective natural immunity that helps block mother-infant transmission of HIV-1.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK	HIV-1 infection	human (DR)	Baier1995
	• Epitope name: P18 • Linked HIV-1 T1 and P18 peptides to anti-HLA-DR and IgD Fab fragments to enhance uptake by antigen presenting cells thus increase immunogenicity				
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK	Vaccine	murine (H-2 A^d)	Takahashi1990
	Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* gp160 • Epitope name: P18 • Induces both class II restricted CD4+ Th cells, and class I restricted CD8+ CTL				
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK	Peptide-HLA interaction	murine (H-2 I-A^d)	Takeshita1995
	• Epitope name: P18 • Binds Class II H-2 I-A^d requiring riqrgPgRaFvti, and Class I H-2 D^d, requiring iGPgRaFvtI				
gp160 (308–322)	Env (IIIB)	RIQRGPRAFVTIGK	Vaccine	murine (H-2^d)	Lu1999
	Vaccine *Vector/Type:* DNA with CMV promotor *Strain:* IIIB *HIV component:* gp160, REV *Adjuvant:* MIP-1 alpha expression vector • Epitope name: P18 • MIP-1a expression plasmid co-inoculated with a DNA vaccine consisting of HIV-1 pCMV160IIIB and pcREV enhanced the HIV-specific T-cell immune response as measured by a CTL test against using V3 peptide pulsed targets, and a DTH test to V3 peptide. • The IgG1/IgG2a response was lowered with co-inoculation of MIP-1 alpha, suggesting it preferentially elicits a Th1 response				
gp160 (308–327)	gp120 (306–325 MN)	RIHIGPGRAFYTTKNIIGIT	HIV-1 infection	human (DRB1*0101)	Hayball1997
	• Tandem repeated presentation of epitope enhances binding to class II molecule and therefore induction of T-cell proliferation • Tandem peptides are thought to enhance proliferation through improved recruiting of CD4 to the activation complex, which can counter-balance gp120's sequestering of CD4 and consequential inhibition of a proliferative response				
gp160 (309–323)	gp120 (309–323 IIIB, B10)	EQRGPGRAFVTIGKI	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				
gp160 (309–325)	gp120 (314–330)	IQRGPGRAFVTIGKIGN	HIV-1 infection	human	Caruso1997
	• As HIV-1-infected individuals progress to disease, T-cells show reduced ability to proliferate in response to HIV antigen, but retain the ability to express the activation antigens CD25 and CD71 • The ability to express activation markers in response to HIV is retained, but the response to tetanus toxoid recall antigen is lost • This study investigated CD25 and CD71 expression in PBMC from patients at various stages of progression, measuring the response to in vitro stimulation by peptide cocktail containing four antigenic Env peptides, or p17 and p24				
gp160 (310–328)	gp120 (310–329 89.6)	SIGPGRAFYARRNIIGDIRQ	Vaccine	murine	Dai2001
	Vaccine *Vector/Type:* recombinant protein *Strain:* 89.6 *HIV component:* gp120 *Adjuvant:* R192G mutant heat-labile toxin from enterotoxigenic E. coli (mLT) • Epitope name: Peptide 29 • Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This peptide was reactive in 2/10 BALB/c mice tested, and in 8/10 CBA/J mice.				
gp160 (311–319)		RGPGRAFVT	Vaccine	murine	Barouch2002
	Vaccine *Vector/Type:* DNA *Strain:* BH10 *HIV component:* gp120 *Adjuvant:* GMCSF (bicistronic) • gp120 encoding DNA co-injected with a plasmid carrying GMCSF gave meager CD4+ T-cell responses in BALB/c mice relative to bicistronic gp120 and GMCSF cloned into the same vector and expressed from the same promoter. • The bicistronic gp120/GM-CSF vaccine induced an approximately 10-fold increase of CD4+ T cell proliferative responses to gp120, as well as a significant increase in IL-2, IL-4, IL-10, IFN-gamma and GM-CSF production, compared to immunization with the monocistronic pVIJ-gp120 with GMCSF. The enhanced proliferative responses were substantiated by CD4+ T-cell Elispot. • Both mono and bicistronic DNA vaccines induced similar CTL responses directed against the H-2Dd restricted P18 peptide RGPRAFTVTI in murine splenocytes despite the enhanced proliferative responses.				
gp160 (311–320)	gp120 (IIIB)	RGPGPAFVTI	Vaccine	murine (H-2^d)	Xin1998
	Vaccine *Vector/Type:* DNA with CMV promotor *Strain:* IIIB *HIV component:* gp160, REV *Adjuvant:* IL-2 expression vector • Intranasal immunization with IL-2 expression plasmid in addition to DNA vaccine amplifies cellular response to antigen, probably via activation of Th type 1 (Th1) cells				
gp160 (311–320)	gp120 (IIIB)	RGPGPAFVTI	Vaccine	murine (H-2^d)	Xin1999
	Vaccine *Vector/Type:* DNA with CMV promotor *Strain:* IIIB *HIV component:* gp160, REV *Adjuvant:* IL-15 expression vector • Intranasal immunization with IL-15 expression plasmid in addition to DNA vaccine increases DTH response and CTL activity to the antigen, and decreases the serum IgG1 to IgG2a ratio, enhancing Th type 1 (Th1) cell-mediated immunity • Expression of IL-2 or IL-15 can enhance Th1 response to the vaccine, but they to do not appear to elicit a synergistic response				
gp160 (311–320)	gp120 (IIIB)	RGPGPAFVTI	Vaccine	murine (H-2^d)	Ihata1999
	Vaccine *Vector/Type:* DNA with CMV promotor *Strain:* IIIB *HIV component:* gp160, REV *Adjuvant:* CD40L expression vector • CD40L expression increases DTH, and Th1-dependent responses based on enhanced IgG2a titers, with no lowering of IgG1 titers • Elispot assay indicated co-injection with hCD40L resulted in greater numbers of IFN-gamma producing Th1cells, as well as increased IL-4 producing Th2 cells • Results suggest hCD40L enhance both Th1 and Th2 cells, and such a pattern of induction is unique among adjuvants, as most adjuvants increase either Th1 or Th2				
gp160 (311–322)	Env (IIIB)	RGPGRAFVTIGK	Vaccine	murine (H-2^d)	Kusakabe2000
	Vaccine *Vector/Type:* DNA with CMV promotor *Strain:* IIIB *HIV component:* gp160, REV *Adjuvant:* pGM-CSF expression vector • The timing of delivery of the pGM-CSF expression plasmid for intramuscular DNA pCMV160IIIB/REV vaccination impacts the Th response, maximizing Th2 responses when administered 3 days prior to the DNA vaccine, and Th1 responses when administered 3 days after the DNA vaccine				
gp160 (314–328)	gp120 (314–328 IIIB, B10)	GRAFVTIGKIGNMRQ	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				
gp160 (314–341)	gp120 (319–346 NL43)	GRAFVTIGKIGNMRQAHCN-ISRAKWNAT	Vaccine	human	Sitz1999
	Vaccine *Vector/Type:* recombinant protein *Strain:* NL43 *HIV component:* gp120, gp160 • There was a great breadth of proliferative response to env peptides in 19 HIV-1 infected rgp160 and 17 HIV-1 infected rgp120 vaccine recipients • More than 25% of vaccinees had a stimulation index of greater than 5 to this peptide				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (315–328)	Env (UG92005)	RAYYTTNIVGNIRQ	Vaccine	murine (H-2 IA^b)	Surman2001
	Vaccine *Vector/Type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Adjuvant:* Freund's adjuvant				
	• This epitope is located in the V3 region of UG92005 (UG, clade D) and was recognized by two hybridomas with Vβ usage not determined, but one used Vα 8				
	• C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant				
	• The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells				
	• Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined				
	• Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO				
	• 80 unique clonotypes were characterized from six mice				
	• H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41).				
	• Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.				
gp160 (317–331)	gp160 (324–338 IIIB)	FVTIGKIGNMRQAHC	Vaccine	murine (H-2^k, H-2^d)	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Adjuvant:* Freund's adjuvant				
	• B10.BR (H-$2A^k$, E^k) and B10.D2 (H-$2A^d$, E^d) mice immunized with rec gp160 showed a proliferative response to this peptide				
	• FVTIGKIGNMRQAHCNISRAKWNNTLKQIDSKL encompasses several murine Th epitopes including FVTIGKIGNMRQAHC and is referred to as a "multideterminant region" or cluster peptide				
gp160 (317–331)	gp120 (324–338 IIIB)	FVTIGKIGNMRQAHC	Vaccine	murine (H-$2^{k,d}$)	Hale1989
	Vaccine *Strain:* IIIB *HIV component:* gp160				
	• Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types				
gp160 (317–336)	gp120 (321–340 MN)	YTTKNIIGTIRQAHCNSRA	Vaccine	guinea pig	Chattergoon2002
	Vaccine *Vector/Type:* protein, DNA *Strain:* MN *HIV component:* gp120 *Adjuvant:* complete Freund's adjuvant (CFA)				
	• Epitope name: 1987				
	• Hartley guinea pigs were intradermally injected with either recombinant protein or plasmid expressed gp120 and monitored for delayed type hypersensivity (DTH) responses after vaccination, which are related to Th1 T-cell responses. CFA did not augment responses in animals vaccinated with plasmid.				
	• A total of 7 gp120 peptides elicited a delayed type hypersensivity (DTH) response after vaccination, out of a set of 60 overlapping peptides that spanned gp120. The vaccine delivery system, DNA versus rec protein, resulted in the recognition of distinct peptides.				
	• 4/5 animals vaccinated with rec gp120 responded by DTH to this peptide, as did 4/6 vaccinated with plasmid gp120 DNA.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (317–349)	gp160 (324–356 IIIB)	FVTIGKIGNMRQAHCNISR-AKWNNTLKQIDSKL	HIV-1 infection, Vaccine	human, murine (H-2^k, H-2^d)	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Adjuvant:* Freund's adjuvant				
	• FVTIGKIGNMRQAHCNISRAKWNNTLKQIDSKL encompasses several murine Th epitopes and is referred to as a "multideterminant region" or cluster peptide				
	• Six multideterminant region cluster peptides were evaluated Th responses in different MHC/HLA backgrounds after vaccination of mice with gp160, or in infected people				
	• This cluster peptide elicited proliferative responses in cells from B10.BR mice (H-2A^k, E^k) and B10.D2 mice (H-2A^d, E^d), but shorter peptides from within this region stimulated H-2^k, H-2^d, H-2^b and H-2^s responses				
	• IL-2 production in response to this peptide was observed in 58% (21/36) of asymptomatic HIV-infected individuals				
gp160 (319–338)	gp120 (320–339 89.6)	RRNIIGDIRQAHCNISRAKW	Vaccine	murine	Dai2001
	Vaccine *Vector/Type:* recombinant protein *Strain:* 89.6 *HIV component:* gp120 *Adjuvant:* R192G mutant heat-labile toxin from enterotoxigenic E. coli (mLT)				
	• Epitope name: Peptide 30				
	• Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences.				
	• This peptide was highly reactive in 7/10 BALB/c mice tested, and in 7/10 CBA/J mice and was consider one of the 3 immunodominant peptides identified that were shared in both mouse strains: RRNIIGDIRQAHCNISRAKW, NNTLQQIVIKLREKFRNKTI, GTNGTEGNDIITLQCRIKQI.				
gp160 (319–338)	gp120 (320–339 89.6)	RRNIIGDIRQAHCNISRAKW	Vaccine	murine (H-2^k, H-2^d)	Dai2001
	Vaccine *Vector/Type:* recombinant protein *Strain:* 89.6 *HIV component:* gp120 *Adjuvant:* mutant R192G heat-labile toxin from E. coli as adjuvant				
	• Promiscuous immunodominant epitopes in gp120 were mapped by overlapping peptides in CBA/J H-2^k and BALB/c H-2^d mice, and all were found to be in the outer domain, proximal to regions of structural disorder indicated by the crystal structure or by sequence divergence.				
	• This peptide was recognized by 7/10 CBA/J and 7/10 BALB/c mice with SI $>$ 4, averaging 6.3 and 4.8, and is considered to be promiscuously immunodominant				
	• Uniquely immunodominant sequences tended to be in the inner domain of the protein				
gp160 (321–336)	gp120 (IIIB)	RIIGDIRKAHCNISRY	in vitro stimulation	human	Manca1995b
	• Peptide stimulation of PBMC from non-infected individuals in vitro				
	• Peptide priming does not always induce T-cells that recognize whole protein				
gp160 (322–336)	Env (1007)	IIGDIRQAHCNISRE	Vaccine	murine (H-2 IA^b)	Surman2001
	Vaccine *Vector/Type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Adjuvant:* Freund's adjuvant				
	• This epitope is located in the V3 region of 1007 (US, clade B) and was recognized by three hybridomas with Vβ usage Vβ 6 and not determined				
	• C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant				
	• The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined • Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO • 80 unique clonotypes were characterized from six mice • H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41). • Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.				
gp160 (322–336)	Env (UG92005)	IVGNIRQAHCNVSKA	Vaccine	murine (H-2 IA^b)	Surman2001
	Vaccine *Vector/Type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Adjuvant:* Freund's adjuvant • This epitope is located in the V3 region of UG92005 (UG, clade D) and was recognized by three hybridomas with Vβ usage Vβ 6, 8.1, and not determined • C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant • The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells • Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined • Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO • 80 unique clonotypes were characterized from six mice • H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41). • Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.				
gp160 (322–336)	Env (UG92005)	IVGNIRQAHCNVSKA	Vaccine	murine (H-2 IA^b)	Surman2001
	Vaccine *Vector/Type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Adjuvant:* Freund's adjuvant • This epitope is located in the V3 region of UG92005 (UG, clade D) and was recognized by three hybridomas with Vβ usage Vβ 6, 8.1, and not determined • C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant • The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells • Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO • 80 unique clonotypes were characterized from six mice • H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41). • Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.				
gp160 (322–341)	gp120 (322–341 IIIB)	KIGNMRQAHCNISRAKWNN-T?	HIV-1 infection	human	Geretti1994
	• Epitope name: F4 • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 1/15 responders recognized this peptide, SI = 7.6.				
gp160 (324–336)	Env (UG92005)	GNIRQAHCNVSKA	Vaccine	murine (H-2 IA^b)	Surman2001
	Vaccine *Vector/Type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Adjuvant:* Freund's adjuvant • This epitope is located in the V3 region of UG92005 (UG, clade D) and was recognized by two hybridoma with Vβ usage Vβ8.2 and not determined • The epitope described here is the region of overlap of two 15 mers that were both able to stimulate IL-2 production from the hybridoma (IVGNIRQAHCNVSKA and GNIRQAHCNVSKAKW) • C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant • The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells • Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined • Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO • 80 unique clonotypes were characterized from six mice • H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41). • Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (324–338)	Env (UG92005)	GNIRQAHCNVSKAKW	Vaccine	murine (H-2 IA^b)	Surman2001

Vaccine *Vector/Type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Adjuvant:* Freund's adjuvant

- This epitope is located in the V3 region of UG92005 (UG, clade D) and was recognized by eleven hybridomas with Vβ usage Vβ5, 7, 8.1, 8.2, 11 and not determined – a Vβ 8.1's and Vβ 8.2 also were shown to use Vα 8, and one of the ND used Vα 2
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO
- 80 unique clonotypes were characterized from six mice
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41).
- Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.

gp160 (327–341)	gp120 (327–341 HXB2)	RQAHCNISRAKWNNT	Vaccine	murine (I-A^d)	Warren1992

Vaccine *Vector/Type:* recombinant protein *Strain:* HXB2 *HIV component:* gp120

- Minimum epitope and MHC restriction determined for CTL clone that recognizes the N-terminal flank of the V3 loop

gp160 (327–346)	gp120 (331–350 MN)	RQAHCNISRAKWNDILRQIV	Vaccine	guinea pig	Chattergoon2002

Vaccine *Vector/Type:* protein, DNA *Strain:* MN *HIV component:* gp120 *Adjuvant:* complete Freund's adjuvant (CFA)

- Epitope name: 1988
- Hartley guinea pigs were intradermally injected with either recombinant protein or plasmid expressed gp120 and monitored for delayed type hypersensivity (DTH) responses after vaccination, which are related to Th1 T-cell responses. CFA did not augment responses in animals vaccinated with plasmid.
- A total of 7 gp120 peptides elicited a delayed type hypersensivity (DTH) response after vaccination, out of a set of 60 overlapping peptides that spanned gp120. The vaccine delivery system, DNA versus rec protein, resulted in the recognition of distinct peptides.
- 4/5 animals vaccinated with rec gp120 responded by DTH to this peptide, and 2/6 responded that were vaccinated with plasmid gp120 DNA.

gp160 (330–350)	gp120 (330–349 IIIB)	HCNISRAKWNNTLKQIASK-LR?	HIV-1 infection	human	Geretti1994

- Epitope name: F5
- Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.
- After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.
- IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• 3/15 responders recognized this peptide, average SI = 5.5.				
gp160 (331–345)	gp120 (IIIB)	CNISRAQWNNTLEQI	in vitro stimulation	human	Manca1995b
	• Peptide stimulation of PBMC from non-infected individuals in vitro • Peptide priming does not always induce T-cells that recognize whole protein				
gp160 (332–354)	gp120 (337–359 NL43)	NISRAKWNATLKQIASKLR-EQFG	Vaccine	human	Sitz1999
	Vaccine *Vector/Type:* recombinant protein *Strain:* NL43 *HIV component:* gp120, gp160 • There was a great breadth of proliferative response to env peptides in 19 HIV-1 infected rgp160 and 17 HIV-1 infected rgp120 vaccine recipients • More than 30% of vaccinees had a stimulation index of greater than 5 to this peptide				
gp160 (335–349)	gp160 (342–356 IIIB)	RAKWNNTLKQIDSKL	Vaccine	murine (H-2^k, H-2^b, H-2^s)	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Adjuvant:* Freund's adjuvant • B10.BR (H-$2A^k$, E^k), B10.A(5R) (H-$2A^b$, E^b) and B10.S(9R) (H-$2A^s$, E^s) mice immunized with rec gp160 showed a proliferative response to this peptide • FVTIGKIGNMRQAHCNISRAKWNNTLKQIDSKL encompasses several murine Th epitopes including RAKWNNTLKQIDSKL and is referred to as a "multideterminant region" or cluster peptide				
gp160 (335–349)	gp120 (342–356 IIIB)	RAKWNNTLKQICSKL	Vaccine	murine (H-$2^{k,t4,i5}$)	Hale1989
	Vaccine *Strain:* IIIB *HIV component:* gp160 • Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types				
gp160 (337–356)	gp120 (341–360 MN)	KWNDTLRQIVSKLKEQFKNK	Vaccine	guinea pig	Chattergoon2002
	Vaccine *Vector/Type:* protein, DNA *Strain:* MN *HIV component:* gp120 *Adjuvant:* complete Freund's adjuvant (CFA) • Epitope name: 1989 • Hartley guinea pig were intradermally injected with either recombinant protein or plasmid expressed gp120 and monitored for delayed type hypersensivity (DTH) responses after vaccination, which are related to Th1 T-cell responses. CFA did not augment responses in animals vaccinated with plasmid. • A total of 7 gp120 peptides elicited a delayed type hypersensivity (DTH) response after vaccination, out of a set of 60 overlapping peptides that spanned gp120. The vaccine delivery system, DNA versus rec protein, resulted in the recognition of distinct peptides. • 3/5 animals vaccinated with rec gp120 responded by DTH to this peptide, and 2/6 responded that were vaccinated with plasmid gp120 DNA.				
gp160 (339–359)	gp120 (340–359 89.6)	NNTLQQIVIKLREKFRNKTI	Vaccine	murine	Dai2001
	Vaccine *Vector/Type:* recombinant protein *Strain:* 89.6 *HIV component:* gp120 *Adjuvant:* R192G mutant heat-labile toxin from enterotoxigenic E. coli (mLT) • Epitope name: Peptide 32 • Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences. • This peptide was reactive in 6/10 BALB/c mice tested, and in 4/10 CBA/J mice and was consider one of the 3 immunodominant peptides identified that were shared in both mouse strains: RRNIIGDIRQAHCNISRAKW, NNTLQQIVIKLREKFRNKTI, GTNGTEGNDIITLQCRIKQI.			
gp160 (339–359)	gp120 (340–359 89.6)	NNTLQQIVIKLREKFRNKTI	Vaccine	murine (H-2^k, H-2^d)	Dai2001
	Vaccine *Vector/Type:* recombinant protein *Strain:* 89.6 *HIV component:* gp120 *Adjuvant:* mutant R192G heat-labile toxin from E. coli as adjuvant				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Promiscuous immunodominant epitopes in gp120 were mapped by overlapping peptides in CBA/J H-2^k and BALB/c H-2^d mice, and all were found to be in the outer domain, proximal to regions of structural disorder indicated by the crystal structure or by sequence divergence. • This peptide was recognized by 4/10 CBA/J and 6/10 BALB/c mice with SI $>$ 4, averaging 4.9 and 5.5 and is considered to be promiscuously immunodominant • Uniquely immunodominant sequences tended to be in the inner domain of the protein				
gp160 (341–356)	gp120 (IIIB)	TLEQIVKKLREQFGNC	in vitro stimulation	human	Manca1995b
	• Peptide stimulation of PBMC from non-infected individuals in vitro • Peptide priming does not always induce T-cells that recognize whole protein				
gp160 (342–361)	gp120 (342–361 IIIB)	LKQIASKLREQFGNNKTII-F?	HIV-1 infection	human	Geretti1994
	• Epitope name: G1 • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 2/15 responders recognized this peptide, average SI = 6.0.				
gp160 (344–357)	gp120 (346–359)	QIVKKLREQFGNNK	HIV-1 infection	human	Krowka1990
	• Conjugation of HIV peptides to liposomes and rIL-2 stimulation may enhance cell-mediated responses				
gp160 (349–368)	gp120 (350–369 89.6)	LREKFRNKTIAFNQSSGGD	Vaccine	murine	Dai2001
	Vaccine *Vector/Type:* recombinant protein *Strain:* 89.6 *HIV component:* gp120 *Adjuvant:* R192G mutant heat-labile toxin from enterotoxigenic E. coli (mLT) • Epitope name: Peptide 33 • Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences. • This peptide was reactive in 3/10 BALB/c mice tested, and in 5/10 CBA/J mice.				
gp160 (350–370)	gp120 (350–370 IIIB)	REQFGNNKTIIFKQSSGGD-PE?	HIV-1 infection	human	Geretti1994
	• Epitope name: G2 • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 1/15 responders recognized this peptide, average SI = 3.2.				
gp160 (353–360)	gp120 (355–362 IIIB)	FGNNKTII	SHIV infection	Rhesus macaque	Lekutis1997a
	• C3 region minimal epitope determined through fine epitope mapping				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Cell line was lost prior to confirmation of MHC requirements				
gp160 (363–372)	gp120 (368–377 LAI) • Stimulates T-cell proliferation in HIV-infected donors	QSSGGDPEIV	HIV-1 infection	human	Schrier1989
gp160 (364–378)	gp120 (364–378 IIIB, B10) • 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.	SSGGKPEIVTHSFNC	HIV-1 infection	human	Wahren1989b, Wahren1989a
gp160 (369–383)	gp120 (369–383 IIIB, B10) • 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.	PEIVTHSFNCGGEFF	HIV-1 infection	human	Wahren1989b, Wahren1989a
gp160 (380–393)	gp120 (380–393 IIIB) • Epitope name: G4 • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • Five peptides were recognized most frequently: C2 (aa 142-161), C3 (aa 152-171), C5 (aa 172-191), E5 (aa 272-291) and G4 (aa 380-393). The first three were in or near V2, the other two were proximal to the V3 and V4 loops. • 4/15 responders recognized this immunodominant peptide, average SI = 4.4.	GEFFYCNSTQLFNS?	HIV-1 infection	human	Geretti1994
gp160 (381–395)	gp120 (IIIB) • Peptide stimulation of PBMC from non-infected individuals in vitro • Peptide priming does not always induce T-cells that recognize whole protein	EFFYCNTTQLFNNTW	in vitro stimulation	human	Manca1995b
gp160 (392–411)	gp120 (392–411 IIIB) • Epitope name: G5 • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 1/15 responders recognized this peptide, SI = 9.3.	NSTWFNSTWSTEGSNNTEG-S?	HIV-1 infection	human	Geretti1994
gp160 (394–408)	gp120 (394–408 IIIB, B10) • 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.	TWFNSTWSTKGSNNT	HIV-1 infection	human	Wahren1989b, Wahren1989a
gp160 (396–411)	gp120 (IIIB) • Peptide stimulation of PBMC from non-infected individuals in vitro • Peptide priming does not always induce T-cells that recognize whole protein	FNNTWRLNHTEGTKGC	in vitro stimulation	human	Manca1995b

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (399–413)	gp120 (399–413 IIIB, B10)	TWSTKGSNNTEGSDT	HIV-1 infection	human	Wahren1989b, Wahren1989a
• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.					
gp160 (404–423)	gp120 (400–419 89.6)	GTNGTEGNDIITLQCRIKQI	Vaccine	murine	Dai2001
Vaccine *Vector/Type:* recombinant protein *Strain:* 89.6 *HIV component:* gp120 *Adjuvant:* R192G mutant heat-labile toxin from enterotoxigenic E. coli (mLT)					
• Epitope name: Peptide 38					
• Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences.					
• This peptide was reactive in 8/10 BALB/c mice tested, and in 6/10 CBA/J mice, and was consider one of the 3 immunodominant peptides identified that were shared in both mouse strains: RRNIIGDIRQAHCNISRAKW, NNTLQQIVIKLREKFRNKTI, GTNGTEGNDIITLQCRIKQI.					
gp160 (404–423)	gp120 (400–419 89.6)	GTNGTEGNDIITLQCRIKQI	Vaccine	murine (H-2^k, H-2^d)	Dai2001
Vaccine *Vector/Type:* recombinant protein *Strain:* 89.6 *HIV component:* gp120 *Adjuvant:* mutant R192G heat-labile toxin from E. coli as adjuvant					
• Promiscuous immunodominant epitopes in gp120 were mapped by overlapping peptides in CBA/J H-2^k and BALB/c H-2^d mice, and all were found to be in the outer domain, proximal to regions of structural disorder indicated by the crystal structure or by sequence divergence.					
• This peptide was recognized by 4/10 CBA/J and 6/10 BALB/c mice with SI $>$ 4, averaging 4.9 and 5.5 and is considered to be promiscuously immunodominant					
• Uniquely immunodominant sequences tended to be in the inner domain of the protein					
gp160 (405–420)	Env (1007)	SNNTVGNPIILPCRI	Vaccine	murine (H-2 IA^b)	Surman2001
Vaccine *Vector/Type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Adjuvant:* Freund's adjuvant					
• This epitope is located in the V4C4 region of 1007 (US, clade B) and was recognized by 13 hybridomas with Vβ usage Vβ 4, 7, 8.1, 8.2, 10, 12 and not determined – one of the Vβ 8.2 was shown to utilize Vα 2					
• C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant					
• The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells					
• Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined					
• Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO					
• 80 unique clonotypes were characterized from six mice					
• H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41).					

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.				
gp160 (410–429)	gp120 (410–429 PV22)	GSDTITLPCRIKQFINMWQE	HIV-1 infection	human (DR4)	Callahan1990
	• Synthetic peptides representing natural variants were used to test for recognition in the context DR4				
gp160 (410–429)	gp120 (410–429 PV22)	GSDTITLPCRIKQFINMWQE	HIV-1 infection	human (DR4(Dw10))	Polydefkis1990
	• Human CD4+ T-cell clones lyse recombinant vaccinia virus-infected cells that synthesize envelope gp160				
gp160 (412–431)	gp120 (412–431 IIIB)	DTITLPCRIKQIINMWQKV-G?	HIV-1 infection	human	Geretti1994
	• Epitope name: H2 • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 1/15 responders recognized this peptide, SI = 5.7.				
gp160 (416–431)	gp120 (IIIB)	LPCRIKQIINMWQEVY	in vitro stimulation	human	Manca1995b
	• Peptide stimulation of PBMC from non-infected individuals in vitro • Peptide priming does not always induce T-cells that recognize whole protein				
gp160 (418–436)	Env (417–435)	CRIKQIINMWQGVGKAMYA	HIV-1 infection	human, chimpanzee	Nehete1998b
	• HIV-infected chimpanzees and HIV-positive patients show positive proliferative responses to multiple peptides from five conserved regions of the HIV-1 Env				
gp160 (421–436)	gp120 (426–441 IIIB)	KQFINMWQEWGKAMYA		human	Furci1997
	• Epitope T1 variant: 9/11 exposed-uninfected individuals in this study had a proliferative response to a C5 peptide, but none reacted with this previously defined epitope • IIIB position 435 listed as W in this epitope as opposed to V in the sequence.				
gp160 (421–436)	gp120 (428–433 IIIB)	KQIINMWQEVGKAMYA	HIV-1 infection	human	Wasik2000
	• Epitope name: T1 • Th responses measured by IL-2 responses to P18 and T1 in HIV-1 infected infants were undetectable at less than 1 month of age, and remained low in children with AIDS symptoms, but increased with age in children with slowly progressive disease • The kinetics and intensity of the CTL activity during the first year of life was related to the child's ability to make Th1 responses				
gp160 (421–436)	gp120 (428–433 IIIB)	KQIINMWQEVGKAMYA	HIV-1 infection	human	Wasik1997
	• Epitope name: T1 • The breadth and intensity of the CTL response and the type of Th response was studied in seven rapidly progressing HIV-1+ infants • IL-2 and γ IFN production from Th1 cells correlated with the CTLp frequency against HIV-1 Gag, Env, Nef and Pol • IL-4 production from Th2 cells was inversely correlated with the CTLp frequency • The HIV-1+ children with strong CTL responses had levels of anti-CD3 MAb induction of Th1 cells comparable to those of uninfected children				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (421–436)	gp120 (428–443 IIIB)	KQIINMWQEVGKAMYA	Vaccine	human	Berzofsky1988
	Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* gp160				
	• Epitope name: T1				
	• Proliferative response to T1 and T2 peptides in 14 immunized, uninfected humans				
gp160 (421–436)	gp120 (428–443 IIIB)	KQIINMWQEVGKAMYA	Vaccine	goat	Palker1989
	Vaccine *Vector/Type:* peptide *Strain:* IIIB				
	• Epitope name: T1				
	• Goats immunized with peptides containing V3 type-specific neutralizing determinants coupled to T1				
gp160 (421–436)	gp120 (428–443 IIIB)	KQIINMWQEVGKAMYA	HIV-1 infection	human	Clerici1989
	• Epitope name: T1				
	• IL-2 production detection of Th lymphocytes from asymptomatic HIV-positive individuals				
gp160 (421–436)	gp120 (428–443 IIIB)	KQIINMWQEVGKAMYA	HIV-1 infection	human	Clerici1991a
	• Epitope name: T1				
	• Peptides stimulate Th cell function and CTL activity in similar patient populations				
gp160 (421–436)	gp120 (428–443 IIIB)	KQIINMWQEVGKAMYA	Vaccine	human	Clerici1991b
	Vaccine *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* gp160				
	• Epitope name: T1				
	• Immunizing uninfected individuals with rgp160 results in stronger Th response than does natural infection				
gp160 (421–436)	gp120 (428–443 IIIB)	KQIINMWQEVGKAMYA		human	Clerici1992
	• Epitope name: T1				
	• Cell-mediated immune response to HIV-1 peptides in HIV-1 exposed seronegative men				
gp160 (421–436)	gp120 (428–443 IIIB)	KQIINMWQEVGKAMYA	Vaccine	murine	diMarzo Veronese1994
	Vaccine *Vector/Type:* bacteriophage coat protein *Strain:* MN *HIV component:* V3				
	• Epitope T1 was engineered into a filamentous bacteriophage coat protein, and the Th epitope stimulated Ab production to the V3 loop				
gp160 (421–436)	gp120 (428–443 IIIB)	KQIINMWQEVGKAMYA	Vaccine	chimpanzee	Haynes1993
	Vaccine *Vector/Type:* peptide *Strain:* IIIB				
	• Epitope name: T1				
	• Hybrid T1-V3 peptide immunogenicity reduced when the fusogenic domain of gp41 was added				
gp160 (421–436)	gp120 (428–443 IIIB)	KQIINMWQEVGKAMYA	HIV-1 infection	human	Clerici1997
	• Epitope name: T1				
	• Used in a study of the influence of pentoxifylline on HIV specific T-cells				
gp160 (421–436)	gp120 (428–443 IIIB)	KQIINMWQEVGKAMYA		human	Pinto1995
	• Epitope name: T1				
	• CTL activity analyzed in parallel with Th reactivity in exposed but uninfected health care workers				
gp160 (421–436)	gp160 (428–433 IIIB)	KQIINMWQEVGKAMYA	HIV-1 infection, HIV-1 exposed seronegative	human	Wasik1999
	• Epitope name: T1				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• IL-2 responses associated with beta-chemokine expression were detectable at birth in the majority of uninfected infants born to HIV+ mothers, declining by age 6 months • T1 peptide: In both uninfected and infected infants of HIV-positive mothers, responses to the T1 peptide were more frequent than responses to P18 (RIQRGPGRAFVTIGK) • T1 is a highly conserved epitope, whereas P18 has a higher mutation rate due to its location in the immunodominant V3 loop region				
gp160 (421–436)	gp120 (428–443 IIIB)	KQIINMWQEVGKAMYA	HIV-1 infection	human	Kaul1999
	• Epitope name: T1 • Kenyan sex workers that remained seronegative were found to frequently have HIV-env peptide specific Th responses detected by an IL-2 assay (11/20 cases) and mucosal genital tract anti-HIV IgA (16/21 cases) • Helper epitopes used in this study were noted to be previously described [Clerici1989], and were not explicitly described in [Kaul1999]				
gp160 (421–436)	gp120 (MN)	KQIINMWQEVGKAMYA	HIV-1 infection, Vaccine	human	Bartlett1998
	Vaccine *Vector/Type:* peptide *Strain:* MN *HIV component:* polyepitope • Epitope name: T1 • C4-V3 PV (polyvalent HIV envelope synthetic peptide immunogen) consisted of T1 helper epitope presented in tandem with a V3 loop CTL epitope from one of four different North American strains • This was a pilot phase I study involving vaccination of ten HIV-infected subjects who were HLA-B7-positive • Enhanced lymphoproliferative response to peptide was observed in 5/8 vaccinees – increase in neutralizing antibody responses in 4/8 vacinees				
gp160 (421–436)	gp120	KQIINMWQEVGKAMYA	HIV-1 infection, HIV-1 exposed seronegative	human	Kuhn2001
	• Epitope name: T1 • In a S. African perinatal transmission study, 33% (33/86) of cord blood samples from infants with seropositive mothers produced T-helper responses (measured by a bioassay measuring IL2 production in a murine cell line and confirmed with a proliferation assay) against a peptide cocktail containing Th epitopes P18 MN, P18 IIIB, T1, T2, and TH4 • The mothers were predominantly infected with subtype C, but the T help response was detectable in a number of cord blood samples despite using peptides based on B subtype reagents. • 3/33 infants with cord blood T help responses to Env were infected *in utero*, 2/33 were lost to follow up, and 28/33 were not infected. 6/53 of the infants with cord blood that was unresponsive to Env peptide stimulation were infected before delivery, and 8/47 contracted HIV intrapartum or via breast-feeding. • Measurable HIV specific T help responses elicited in the immunologically immature newborn, possibly in response to *in utero* exposure, are associated with a protective natural immunity that helps block mother-infant transmission of HIV-1.				
gp160 (421–436)	gp120 (428–443 RF)	KQIINMWQEVGKAMYA	HIV-1 infection		deLorimier1994
	• Epitope name: T1 • Proton NMR spectroscopy was employed to analyze the solution conformation of a hybrid peptide, T1-SP10RF, in order to better understand the immunogenicity of its' T helper (KQIINMWQEVGKAMYA, CTRPNNNTRKSI), CTL (SITKGPGRVIYATG) and B-cell epitopes (RKSITKGPGRVIYATG). • As a free peptide, the T1 segment, a T-helper epitope is in an extended conformation with nascent helical conformation. It may form a beta strand in native gp120, and a nonnative conformation may account for the inability of free T1 peptide to elicit antibody responses, in contrast to the T1 segment in native gp120. It lacks random-coil conformations, and it is suggested that this may make the peptide less susceptible to complete proteolytic degredation, and be favored within epitopes.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (421–436)	gp120 (428–443 IIIB)	KQIINMWQEVGKAMYA	HIV-1 infection	human (DR)	Baier1995
	• Epitope name: T1 • Linked HIV-1 T1 and P18 peptides to anti-HLA-DR and anti-IgD Fab fragments to enhance uptake by antigen presenting cells and thus increase immunogenicity				
gp160 (421–436)	Env (421–436 IIIB)	KQIINMWQEVGKAMYA	Vaccine	murine (Ek)	Ahlers2001
	Vaccine *Vector/Type:* peptide *Strain:* modified IIIB *HIV component:* Env • Epitope name: T1 • BALB/c and A.AL were immunized with an Env-peptide vaccine construct containing the CTL epitope P18IIIB and a T helper epitope. • Substitution of Glu (wt) to Ala, kqiinmwqAvgkamya, caused increased affinity for MHC class II Ek. This resulted in the upregulation of CD40L in the responding Th cells, and shifted the response towards Th1. Increased Th responses stimulated DCs to produce higher levels of IL-12, and B7-1 and B7-2, thus enhance CTL responses. • The modified epitope, T1A, elicited stronger protection against increasing doses of viral challenge with vaccinia expressing HIV-1 IIIB gp120 compared to the wildtype epitope T1.			
gp160 (421–436)	gp120 (428–443 IIIB)	KQIINMWQEVGKAMYA	Vaccine	murine (H-2$E\alpha E\beta^k$)	Boehncke1993
	Vaccine *Vector/Type:* peptide *Strain:* IIIB • Epitope name: T1 • C3H H2^k mice were used for immunization in the study because H-2^k mice are particularly good T1 responders – T1 can be presented by $E\alpha E\beta^k$ but not $E\alpha E\beta^b$ – the nature of the T1 class II molecular interaction was thoroughly explored • Alanine substitutions across peptide did not negatively affect MHC binding or effective presentation of epitope, except at three critical residues (432N, 435Q, 439K), however substitutions with larger side chains often diminished activity – only a few amino acids were found to be critical for class II interaction and for maintaining T-cell receptor specificity • A gain in potency was observed when 436E was replaced with A, suggesting that substitutions in positions that interfere with binding might allow the design of a more potent vaccine			
gp160 (421–436)	gp120 (428–443 IIIB)	KQIINMWQEVGKAMYA	Vaccine	murine (H-2^d)	Klinman1995
	Vaccine *Vector/Type:* peptide *Strain:* IIIB • Epitope name: T1 • Hybrid T1-V3 peptide activates IL-4 and IL-6 in a dose dependent manner				
gp160 (421–436)	gp160 (428–443 IIIB)	KQIINMWQEVGKAMYA	Vaccine	murine (H-2^k, H-2^s, H-2^d)	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Adjuvant:* Freund's adjuvant • B10.BR (H-2A^k, E^k), B10.D2 (H-2A^d, E^d) and B10.S(9R) (H-2A^s, E^s) mice immunized with rec gp160 showed a proliferative response to this peptide • KQIINMWQEVGKAMYAPPISGQIR encompasses several murine Th epitopes including KQIINMWQEVGKAMYA and is referred to as a "multideterminant region" or cluster peptide			
gp160 (421–436)	gp120 (428–443 IIIB, B10)	KQIINMWQEVGKAMYA	computer prediction	murine (H-2^{k,d,s})	Cease1987
	• Epitope name: T1 • 1 of 2 functional epitopes identified using an amphipathic helix epitope prediction algorithm				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (421–436)	gp120 (428–443 IIIB)	KQIINMWQEVGKAMYA	Vaccine	murine (H-$2^{k,d,t4}$)	Hale1989
	Vaccine *Strain:* IIIB *HIV component:* gp160				
	• Epitope name: T1				
	• Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types				
gp160 (421–436)	gp120 (428–443 IIIB)	KQIINMWQEVGKAMYA	Vaccine	murine (H-2^{k})	Ahlers1997b
	Vaccine *Vector/Type:* peptide *Strain:* IIIB *HIV component:* polyepitope				
	• Epitope name: T1				
	• first identified Th epitope in HIV				
	• Alanine at position 436 (instead of E in wild-type) enhances MHC binding and antigenicity of peptide by several orders of magnitude				
	• Vaccines with a CTL epitope linked to a more potent helper epitope yielded greatly enhanced CTL response relative to the wildtype helper epitope				
	• T1 peptide linked to CTL epitopes in four vaccine constructs used to immunize mice: KQIINMWQEVGKAMYAPPISGQIRRIQRGPGRAFVTIGK, KQIINMWQEVGKAMYAPPISGQIRRIQRGPGRAFVTI, KQIINMWQAVGKAMYAPPISGQIRRIQRGPGRAFVTIGK, KQIINMWQAVGKAMYAPPISGQIRRIQRGPGRAFVTI				
gp160 (421–444)	gp160 (428–451 IIIB)	KQIINMWQEVGKAMYAPPI–SGQIR	HIV-1 infection, Vaccine	human, murine (H-2^{k}, H-2^{b}, H-2^{s}, H-2^{d})	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Adjuvant:* Freund's adjuvant				
	• KQIINMWQEVGKAMYAPPISGQIR encompasses several murine Th epitopes and is referred to as a "multideterminant region" or cluster peptide				
	• Six multideterminant region cluster peptides were evaluated Th responses in different MHC/HLA backgrounds after vaccination of mice with gp160, or in infected people				
	• This cluster peptide elicited proliferative responses in cells from all H-2 haplotypes tested: B10.BR mice (H-$2A^{k}$, E^{k}), B10.D2 mice (H-$2A^{d}$, E^{d}), B10.A(5R) mice (H-$2A^{b}$, E^{b}), and B10.S(9R) mice (H-$2A^{s}$, E^{s})				
	• IL-2 production in response to this peptide was observed in 73% (8/11) of asymptomatic HIV-infected individuals				
gp160 (421–444)	gp120 (428–451 IIIB)	KQIIMNWQEVGKAMYAPPI–SGQIR	Vaccine	murine (H2^{d})	Shirai1996a
	Vaccine *Vector/Type:* peptide *Strain:* IIIB				
	• Epitope name: T1				
	• Linked to a CTL epitope from hepatitis C virus, induced CD4+ helper cells producing IL-2				
gp160 (423–440)	gp120 (428–445)	FINMWQEVGKAMYAPPIS	HIV-1 infection	human	Caruso1997
	• As HIV-1-infected individuals progress to disease, T-cells show reduced ability to proliferate in response to HIV antigen, but retain the ability to express the activation antigens CD25 and CD71				
	• The ability to express activation markers in response to HIV is retained, but the response to tetanus toxoid recall antigen is lost				
	• This study investigated CD25 and CD71 expression in PBMC from patients at various stages of progression, measuring the response to in vitro stimulation by peptide cocktail containing four antigenic Env peptides, or p17 and p24				
gp160 (424–438)	gp120 (424–438 IIIB, B10)	INMWQEVGKAMYAPP	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (425–439)	gp160 (432–446 IIIB)	NMWQEVGKAMYAPPI	Vaccine	murine (H-2^s)	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Adjuvant:* Freund's adjuvant • B10.S(9R) (H-$2A^s$, E^s) mice immunized with rec gp160 showed a proliferative response to this peptide • KQIINMWQEVGKAMYAPPISGQIR encompasses several murine Th epitopes including NMWQEVGKAMYAPPI and is referred to as a "multideterminant region" or cluster peptide				
gp160 (425–439)	gp120 (432–446 IIIB)	NMWQEVGKAMYAPPI	Vaccine	murine (H-2^{t4})	Hale1989
	Vaccine *Strain:* IIIB *HIV component:* gp160 • Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types				
gp160 (426–441)	gp120 (IIIB)	MWQEVGKAMYAPPIGC	in vitro stimulation	human	Manca1995b
	• Peptide stimulation of PBMC from non-infected individuals in vitro • Peptide priming does not always induce T-cells that recognize whole protein				
gp160 (430–444)	gp160 (437–451 IIIB)	VGKAMYAPPISGQIR	Vaccine	murine (H-2^k, H-2^b, H-2^s, H-2^d)	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Adjuvant:* Freund's adjuvant • This peptide elicited proliferative responses in cells from all H-2 haplotypes tested: B10.BR mice (H-$2A^k$, E^k), B10.D2 mice (H-$2A^d$, E^d), B10.A(5R) mice (H-$2A^b$, E^b), and B10.S(9R) mice (H-$2A^s$, E^s) • KQIINMWQEVGKAMYAPPISGQIR encompasses several murine Th epitopes including VGKAMYAPPISGQIR and is referred to as a "multideterminant region" or cluster peptide				
gp160 (430–444)	gp120 (437–451 IIIB)	VGKAMYAPPISGQIR	Vaccine	murine (H-$2^{k,d,i5,t4}$)	Hale1989
	Vaccine *Strain:* IIIB *HIV component:* gp160 • Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types				
gp160 (430–453)	gp120 (430–453)	VGKAMYAPPISGQIRCSSN-ITGLL	Vaccine	murine (H-2^b)	Sjolander1996
	Vaccine *Vector/Type:* recombinant protein *HIV component:* gp160 • Study demonstrates that T-cell determinants from glycoproteins can depend on the glycosylation of the protein • Peptide stimulation of an in vitro proliferative response required in vivo priming with glycosylated protein • Local glycosylation sites thought not to be part of the epitope, but may be important for epitope processing				
gp160 (432–451)	gp120 (432–451 IIIB)	KAMYAPPISGQIRCSSNIT-G?	HIV-1 infection	human	Geretti1994
	• Epitope name: H4 • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 1/15 responders recognized this peptide, SI = 6.3.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (433–447)	Env (UG92005)	AMYAPPIAGLIQCSS	Vaccine	murine (H-2 IA^b)	Surman2001
	Vaccine *Vector/Type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Adjuvant:* Freund's adjuvant				
	• This epitope is located in the C4 region of UG92005 (UG, clade D) and was recognized by ten hybridomas with Vβ usage Vβ 6, 8.1, 8.2, 13, 14 and not determined – among the ND Vβ set, three Vαs were identified, Vα 2, 8, and 11				
	• C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant				
	• The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells				
	• Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined				
	• Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO				
	• 80 unique clonotypes were characterized from six mice				
	• H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41).				
	• Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.				
gp160 (436–451)	gp120 (IIIB)	APPIGGQISCSSNITY	in vitro stimulation	human	Manca1995b
	• Peptide stimulation of PBMC from non-infected individuals in vitro				
	• Peptide priming does not always induce T-cells that recognize whole protein				
gp160 (438–460)	gp120 (443–465 NL43)	PISGQIRCSSNITGLLLTR-DGGN	Vaccine	human	Sitz1999
	Vaccine *Vector/Type:* recombinant protein *Strain:* NL43 *HIV component:* gp120, gp160				
	• There was a great breadth of proliferative response to env peptides in 19 HIV-1 infected rgp160 and 17 HIV-1 infected rgp120 vaccine recipients				
	• Close to 40% of vaccinees had a stimulation index of greater than 5 to this peptide				
gp160 (439–448)	gp120 (151–160 W6.ID)	IGGQIRCSSN	Vaccine	human	Jones1999
	Vaccine *Vector/Type:* recombinant protein *Strain:* W61D *HIV component:* gp120 *Adjuvant:* QS21/MPL adjuvant				
	• HIV-1 specific T-cell lines isolated from an HIV seronegative volunteer vaccinated with rgp120 and a QS21/MPL adjuvant				
	• One T-cell line responds to two overlapping peptides, and the region of overlap is IGGQIRCSSN				
	• The IIIB version of the first reactive peptide, EVGKAMYAPPIGGQIRCSSN, has a single substitution and induces proliferation as well as the original W61D peptide: evgkamyappiSgqircssn.				
gp160 (446–461)	gp120 (IIIB)	SSNITGLLLTRDGGTC	in vitro stimulation	human	Manca1995b
	• Peptide stimulation of PBMC from non-infected individuals in vitro				
	• Peptide priming does not always induce T-cells that recognize whole protein				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (452–471)	gp120 (452–471 IIIB)	LLLTRDGGNSNNESEIFRP-G?	HIV-1 infection	human	Geretti1994
	• Epitope name: I1 • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 2/15 responders recognized this peptide, average SI = 3.5.				
gp160 (456–470)	gp120 (IIIB)	RDGGTNVTNDTEVFRC	in vitro stimulation	human	Manca1995b
	• Peptide stimulation of PBMC from non-infected individuals in vitro • Peptide priming does not always induce T-cells that recognize whole protein				
gp160 (459–473)	gp120 (459–473 IIIB, B10)	GNSNNESEIFRPGGG	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				
gp160 (468–483)	gp120 (466–481)	FRPGGGDMRDNWRSEL	HIV-1 infection	human	Krowka1990
	• Conjugation of HIV peptides to liposomes and rIL-2 stimulation may enhance cell-mediated responses				
gp160 (472–491)	gp120 (472–491 IIIB)	GGDMRDNWRSELYKYKVVK-I?	HIV-1 infection	human	Geretti1994
	• Epitope name: I3 • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 2/15 responders recognized this peptide, average SI = 7.2.				
gp160 (474–488)	gp120 (474–488 IIIB, B10)	DMRDNWRSELYKYKV	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				
gp160 (476–490)	gp160 (483–497 IIIB)	RDNWRSELYKYKVVK	Vaccine	murine (H-2^k, H-2^s)	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Adjuvant:* Freund's adjuvant • This peptide elicited proliferative responses in B10.BR mice (H-$2A^k$ and B10.S(9R) mice (H-$2A^s$, E^s) • RDNWRSELYKYKVVKIEPLGVAPT encompasses several murine Th epitopes including RDNWRSELYKYKVVK and is referred to as a "multideterminant region" or cluster peptide				
gp160 (476–490)	gp120 (483–497 IIIB)	RDNWRSELYKYKVVK	Vaccine	murine (H-$2^{d,t4}$)	Hale1989
	Vaccine *Strain:* IIIB *HIV component:* gp160				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types				
gp160 (476–499)	gp160 (483–506 IIIB)	RDNWRSELYKYKVVKIEPL-GVAPT	HIV-1 infection, Vaccine	human, murine (H-2^k, H-2^b, H-2^s, H-2^d)	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Adjuvant:* Freund's adjuvant • RDNWRSELYKYKVVKIEPLGVAPT encompasses several murine Th epitopes and is referred to as a "multideterminant region" or cluster peptide • Six multideterminant region cluster peptides were evaluated Th responses in different MHC/HLA backgrounds after vaccination of mice with gp160, or in infected people • This cluster peptide elicited proliferative responses in cells from all H-2 haplotypes tested: B10.BR mice (H-2A^k, E^k), B10.D2 mice (H-2A^d, E^d), B10.A(5R) mice (H-2A^b, E^b), and B10.S(9R) mice (H-2A^s, E^s) • IL-2 production in response to this peptide was observed in 52% (14/27) of asymptomatic HIV-infected individuals			
gp160 (479–498)	gp120 (481–500 MN)	WRSELYKYKVVTIEPLGVAP	Vaccine	guinea pig	Chattergoon2002
	Vaccine *Vector/Type:* protein, DNA *Strain:* MN *HIV component:* gp120 *Adjuvant:* complete Freund's adjuvant (CFA) • Epitope name: 2013 • Hartley guinea pigs were intradermally injected with either recombinant protein or plasmid expressed gp120 and monitored for delayed type hypersensivity (DTH) responses after vaccination, which are related to Th1 T-cell responses. CFA did not augment responses in animals vaccinated with plasmid. • A total of 7 gp120 peptides elicited a delayed type hypersensivity (DTH) response after vaccination, out of a set of 60 overlapping peptides that spanned gp120. The vaccine delivery system, DNA versus rec protein, resulted in the recognition of distinct peptides. • 0/5 animals vaccinated with rec gp120 responded by DTH to this peptide, while 6/6 vaccinated with plasmid gp120 DNA responded.			
gp160 (482–501)	gp120 (482–501 IIIB)	ELYKYKVVKIEPLGVAPTKA	Vaccine	Rhesus macaque	Lekutis1997b
	Vaccine *Vector/Type:* DNA *Strain:* IIIB *HIV component:* ENV • HIV-1 env DNA vaccine induced Th cell response to this epitope in a rhesus monkey • Epitope was recognized by both monkeys used in this study				
gp160 (482–501)	gp120 (482–501 IIIB)	ELYKYKVVKIEPLGVAPTK-A?	HIV-1 infection	human	Geretti1994
	• Epitope name: I4 • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 3/15 responders recognized this peptide, average SI = 6.0.				
gp160 (483–502)	gp120 (480–499 89.6)	LYKYKVVRIEPIGVAPTRAK	Vaccine	murine	Dai2001
	Vaccine *Vector/Type:* recombinant protein *Strain:* 89.6 *HIV component:* gp120 *Adjuvant:* R192G mutant heat-labile toxin from enterotoxigenic E. coli (mLT) • Epitope name: Peptide 46 • Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences.			

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This peptide was reactive in 7/10 BALB/c mice tested, and in only 1/10 CBA/J mice.				
gp160 (484–496)	gp120 (484–496 HXB2)	YKYKVVKIEPLGV	Vaccine	Rhesus macaque (DR*W201)	Lekutis1998
	Vaccine *Vector/Type:* DNA *Strain:* HXB2 *HIV component:* ENV • Variants of this epitope with substitutions at position 490(K) retained ability to bind to MHC class II, but failed to induce proliferation/cytokine secretion in HIV-1 env-specific CD4+ Th cells • The modified peptide antagonized the wildtype peptide-induced proliferative response				
gp160 (484–498)	gp120 (484–498 IIIB, B10)	YKYKVVKIEPLGVAP	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				
gp160 (484–499)	gp120 (492–506 IIIB)	CKYKVVKIEPLGVAPT	Vaccine	murine (H-$2^{d,k,t4,i5}$)	Hale1989
	Vaccine *Strain:* IIIB *HIV component:* gp160 • Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types				
gp160 (485–499)	gp160 (492–506 IIIB)	KYKVVKIEPLGVAPT	Vaccine	murine (H-2^k, H-2^b, H-2^s, H-2^d)	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Adjuvant:* Freund's adjuvant • This peptide elicited proliferative responses in cells from all H-2 haplotypes tested: B10.BR mice (H-$2A^k$, E^k), B10.D2 mice (H-$2A^d$, E^d), B10.A(5R) mice (H-$2A^b$, E^b), and B10.S(9R) mice (H-$2A^s$, E^s) • RDNWRSELYKYKVVKIEPLGVAPT encompasses several murine Th epitopes including KYKVVKIEPLGVAPT and is referred to as a "multideterminant region" or cluster peptide				
gp160 (485–500)	gp120 (IIIB)	KYKVIKIEPLGIAPTC	in vitro stimulation	human	Manca1995b
	• Peptide stimulation of PBMC from non-infected individuals in vitro • Peptide priming does not always induce T-cells that recognize whole protein				
gp160 (486–494)	gp120 (486–494 IIIB)	YKVVKIEPL	SHIV infection	Rhesus macaque (DRB*W201)	Lekutis1997a
	• C5 region minimal epitope determined through fine epitope mapping				
gp160 (487–512)	gp120 (494–518 IIIB)	KVVKIEPLGVAPTKAKRRV-VQREKRC	Vaccine	murine	Goodman-Snitkoff1990
	Vaccine *Vector/Type:* peptide *Strain:* IIIB • Identification of putative Th epitopes that stimulate an antibody response in peptide immunized mice				
gp160 (492–512)	gp120 (492–512 IIIB)	EPLGVAPTKAKRRVVQREK-RA?	HIV-1 infection	human	Geretti1994
	• Epitope name: I5 • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• 1/15 responders recognized this peptide, SI = 4.9.				
gp160 (493–511)	gp120 (490–508 89.6)	PIGVAPTRAKRRTVQREKR	Vaccine	murine	Dai2001
	Vaccine *Vector/Type:* recombinant protein *Strain:* 89.6 *HIV component:* gp120 *Adjuvant:* R192G mutant heat-labile toxin from enterotoxigenic E. coli (mLT) • Epitope name: Peptide 47 • Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences. • This peptide was reactive in only 2/10 BALB/c mice tested, and in 8/10 CBA/J mice.				
gp160 (499–511)	gp120 (IIIB)	TKAKRRVVEREKR	in vitro stimulation	human (DR)	Wilson1997b
	• Thought to be a mimic of a HLA class II DR β chain variable region • Response to this epitope may cause a breakdown of self-tolerance • Presentation of epitope induced autoreactive T-cell lines in PBMC from uninfected donors • Suppression of proliferation to soluble antigens by the CD8+ fraction of TKAKRRVVEREKR stimulated T-cells was observed				
gp160 (519–543)	Env (519–543)	FLGFLGAAGSTMGAASLTL-TVQARC	Vaccine	Rhesus macaque	Nehete1993
	Vaccine *Vector/Type:* peptide • Synthetic peptide derived from conserved region of the HIV-1 envelope that stimulates a proliferative response in mice, and in rhesus monkeys • Proliferative response to this peptide was observed in 3/3 immunized rhesus monkeys				
gp160 (519–543)	Env (519–543)	FLGFLGAAGSTMGAASLTL-TVQARQ	HIV-1 infection	human, chimpanzee	Nehete1998b
	• HIV-infected chimpanzees and HIV-positive patients show positive proliferative responses to multiple peptides from five conserved regions of the HIV-1 Env				
gp160 (519–543)	gp41 (519–543)	FLGFLGAAGSTMGAASLTL-TVQARC	Vaccine	murine (H-$2^{bxk,sxd}$)	Sastry1991
	Vaccine *Vector/Type:* peptide • Peptides induced T-cell proliferative response to immunizing peptide and to gp160				
gp160 (547–561)	gp41 (547–561 IIIB, B10)	GIVQQQNNLLRAIEA	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				
gp160 (562–576)	gp41 (562–576 IIIB, B10)	QQHLLQLTVWGIKQL	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				
gp160 (572–591)	gp41 (572–591)	GIKQLQARILAVERYLKDQQ	Vaccine	murine (H-$2^{d,b}$)	Brown1995
	Vaccine *Vector/Type:* peptide • This peptide was a good immunogen in BALB/c and CBA mice, producing a strong proliferative response • At least one of the four residues GIKQ enhances stimulation, and in CBA mice these residues influence the ability to prime T-cells in vivo				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• QLQARILAVERY stimulated the greatest in vitro T-cell response • VERYLKDQQ was the minimal reactive sequence recognized by a T-cell line				
gp160 (576–591)	gp41 (576–591) **Vaccine** *Vector/Type:* peptide • This peptide was a poor immunogen in BALB/c and CBA mice used in this experiment, producing a weak proliferative response	LQARILAVERYLKDQQ	Vaccine	murine (H-$2^{d,b}$)	Brown1995
gp160 (578–608)	gp41 (585–615 IIIB) **Vaccine** *Vector/Type:* peptide • Identification of putative Th epitopes that can stimulate an antibody response in peptide immunized mice	ARILAVERYLKDQQLLGIW-GCSGKLICTTAV	Vaccine	murine	Goodman-Snitkoff1990
gp160 (579–601)	gp41 (579–601) **Vaccine** *Vector/Type:* peptide • This peptide was a good immunogen in BALB/c and CBA • This peptide produced a strong Th response in both mice strains which was more responsive towards GIKQLQARILAVERYLKDQQ and LQARILAVERYLKDQQ than to immunizing peptide	RILAVERYLKDQQLLGGIW-GCSGK	Vaccine	murine (H-$2^{d,b}$)	Brown1995
gp160 (579–604)	gp41 (584–609 LAI) • Stimulates T-cell proliferation in HIV-infected donors	RILAVERYLKDQQLLGIWG-CSGKLIC	HIV-1 infection	human	Schrier1989
gp160 (586–597)	Env (586–598) • HIV-infected chimpanzees and HIV-positive patients show positive proliferative responses to multiple peptides from five conserved regions of the HIV-1 Env	YLRDQQLLGIWG	HIV-1 infection	human, chimpanzee	Nehete1998b
gp160 (586–598)	Env (586–598) **Vaccine** *Vector/Type:* peptide • Synthetic peptide derived from conserved region of the HIV-1 envelope that stimulates a proliferative response in mice • Proliferative response to this peptide was observed in 1/3 immunized rhesus monkeys, with a weak transient response in the other two	YLRDQQLLGIWGC	Vaccine	murine, Rhesus macaque	Nehete1993
gp160 (593–604)	gp41 (593–604 IIIB) • Elicits T-cell proliferation and B cell responses, but only during the asymptomatic phase of HIV infection	LGIWGCSGKLIC	HIV-1 infection	human	Bell1992
gp160 (593–604)	gp41 (598–609 LAV-1) • Murine T-dependent B-cell response – 7/29 had a proliferative response to this peptide	LGLWGCSGKLIC	Vaccine	murine ($H2^{d}$)	Schrier1988
gp160 (594–603)	gp41 (594–603 IIIB) • Epitope documented as a "previously described' epitope [Bell1992], but in Bell *et al.* it was described as gp41(594-603 IIIB), LGIWGCSGKLIC. • Immunization with a p24-VLP virus-like particle did not significantly impact CD4+ lymphocyte count, viral load, or p24 antibody titre • Immunization with p24-VLP did not increase the proliferative response to this gp41 epitope, however, there was a modest, short-lived increased proliferative response to p24	GIWGCSGKLI	HIV-1 infection	human	Kelleher1998b
gp160 (594–604)	gp41 (consensus) • Core region of peptides that can stimulate proliferative responses from seronegative and seropositive people	GIWGCSGKLIC	HIV-1 infection	human	Mutch1994

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (598–609)	gp41 (603–614 LAI)	CSGKLICTTAVP	HIV-1 infection	human	Schrier1989
	• Stimulates T-cell proliferation in HIV-infected donors				
gp160 (604–615)	gp41 (609–620 LAI)	CTTAVPWNASWS	HIV-1 infection	human	Schrier1989
	• Stimulates T-cell proliferation in HIV-infected donors				
gp160 (606–620)	gp41 (UG92005)	TNVPWNASWSNKSLE	Vaccine	murine (H-2 IA^b)	Surman2001
	Vaccine *Vector/Type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Adjuvant:* Freund's adjuvant				
	• This gp140 epitope of UG92005 (UG, clade D) was recognized by five hybridomas with Vβ usage Vβ 8.1, 14 and not determined – one of the Vβ 8.1 was shown to utilize Vα 8				
	• C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant				
	• The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells				
	• Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined				
	• Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO				
	• 80 unique clonotypes were characterized from six mice				
	• H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41).				
	• Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.				
gp160 (609–616)	gp41 (consensus)	PWNASWSN	HIV-1 infection	human	Mutch1994
	• Core region of peptides that can stimulate proliferative responses from seronegative and seropositive people				
gp160 (611–620)	gp41 (1007, UG92005)	NASWSNKSLE	Vaccine	murine (H-2 IA^b)	Surman2001
	Vaccine *Vector/Type:* DNA, vaccinia, recombinant protein *Strain:* 1007 (clade B), UG92005 (clade D) *HIV component:* gp140 *Adjuvant:* Freund's adjuvant				
	• This gp41 epitope is conserved in 1007 (US, clade B) and UG92005 (UG, clade D) and was recognized by two hybridomas from two different mice that were vaccinated with different clades – the Vβ usage was Vβ 4 and 14				
	• The epitope described here is the region of overlap of two 15 mers that were both able to stimulate IL-2 production from the hybridoma (T[TN]VPWNASWSNKSLE and NASWSNKSLEQIWNN) – the only difference between 1007 and UG92005 for these two proteins is that 1007 has a T and UG92005 has an N in the second position of the first peptide				
	• C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant				
	• The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined • Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO • 80 unique clonotypes were characterized from six mice • H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41). • Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.				
gp160 (614–629)	gp41 (IIIB)	WSNKSLEDIWDNMTWC	in vitro stimulation	human	Manca1995b
	• Peptide stimulation of PBMC from non-infected individuals in vitro • Peptide priming does not always induce T-cells that recognize whole protein				
gp160 (634–649)	gp41 (IIIB)	EIDNYTNTIYTLLEEC	in vitro stimulation	human	Manca1995b
	• Peptide stimulation of PBMC from non-infected individuals in vitro • Peptide priming does not always induce T-cells that recognize whole protein				
gp160 (647–661)	gp41 (647–661 IIIB, B10)	EESQNQQEKNEQELL	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				
gp160 (650–662)	gp41 (655–667 LAI)	QNQQEKNEQELLE	HIV-1 infection	human	Schrier1989
	• Stimulates T-cell proliferation in HIV-infected donors				
gp160 (667–681)	gp41 (667–681 IIIB, B10)	ASLWNWFNITNWLWY	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				
gp160 (682–696)	gp41 (682–696 IIIB, B10)	IKLFIMIVGGLVGLR	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				
gp160 (724–745)	gp41 (731–752)	PRGPDRPEGIEEEGGERDR-DRS	Vaccine	murine (H-2^k)	McInerney1999
	Vaccine *Vector/Type:* peptide in cowpea mosaic virus (CPMV) *HIV component:* gp41 *Adjuvant:* adjuvant Quil A • A gp41 peptide was expressed in a cowpea mosaic virus (CPMV) and mice were vaccinated with a purified chimeric particle – out of five adjuvants tested, only Quil A could stimulate anti-gp41 antibodies and an in vitro proliferative response • The antibodies were predominantly IgG2a, suggesting a Th1 response				
gp160 (732–744)	gp41 (737–749 LAI)	GIEEEGGERDRDR	HIV-1 infection	human	Schrier1989
	• Stimulates T-cell proliferation in HIV-infected donors				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (780–794)	gp160 (787–801 IIIB)	RIVELLGRRGWEALK	Vaccine	murine (H-2^k, H-2^d, H-2^s)	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Adjuvant:* Freund's adjuvant • This peptide elicited proliferative responses in cells from B10.BR mice (H-2A^k, E^k), B10.D2 mice (H-2A^d, E^d), and B10.S(9R) mice (H-2A^s, E^s) • RIVELLGRRGWEALKYWWNLLQYWSQELKNSAVS encompasses several murine Th epitopes including RIVELLGRRGWEALK and is referred to as a "multideterminant region" or cluster peptide, but the longer peptide only stimulates cells from H-2^k mice				
gp160 (780–794)	gp41 (787–801 IIIB)	RIVELLGRRGWEALK	Vaccine	murine (H-2^{d,k,t4})	Hale1989
	Vaccine *Strain:* IIIB *HIV component:* gp160 • Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types				
gp160 (780–813)	gp160 (787–820 IIIB)	RIVELLGRRGWEALKYWWN-LLQYWSQELKNSAVS	HIV-1 infection, Vaccine	murine (H-2^k)	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Adjuvant:* Freund's adjuvant • RIVELLGRRGWEALKYWWNLLQYWSQELKNSAVS encompasses several murine Th epitopes and is referred to as a "multideterminant region" or cluster peptide • Six multideterminant region cluster peptides were evaluated Th responses in different MHC/HLA backgrounds after vaccination of mice with gp160, or in infected people • This cluster peptide elicited proliferative responses in cells from only B10.BR mice (H-2A^k, E^k), and not from B10.D2 mice (H-2A^d, E^d), B10.A(5R) mice (H-2A^b, E^b), or B10.S(9R) mice (H-2A^s, E^s) • IL-2 production in response to this peptide was observed in 59% (17/29) of asymptomatic HIV-infected individuals				
gp160 (794–808)	gp160 (801–815 IIIB)	KYWWNLLQYWSQELK	Vaccine	murine (H-2^k, H-2^d, H-2^s)	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Adjuvant:* Freund's adjuvant • This peptide elicited proliferative responses in cells from B10.BR mice (H-2A^k, E^k), B10.D2 mice (H-2A^d, E^d), and B10.S(9R) mice (H-2A^s, E^s) • RIVELLGRRGWEALKYWWNLLQYWSQELKNSAVS encompasses several murine Th epitopes including KYWWNLLQYWSQELK and is referred to as a "multideterminant region" or cluster peptide, but the longer peptide only stimulates cells from H-2^k mice				
gp160 (794–808)	gp41 (801–815 IIIB)	KYWWNLLQYWSQELK	Vaccine	murine (H-2^k)	Hale1989
	Vaccine *Strain:* IIIB *HIV component:* gp160 • Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types				
gp160 (799–813)	gp160 (806–820 IIIB)	LLQYWSQELKNSAVS	Vaccine	murine (H-2^k, H-2^d, H-2^s)	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Adjuvant:* Freund's adjuvant • This peptide elicited proliferative responses in cells from B10.BR mice (H-2A^k, E^k), B10.D2 mice (H-2A^d, E^d), and B10.S(9R) mice (H-2A^s, E^s) • RIVELLGRRGWEALKYWWNLLQYWSQELKNSAVS encompasses several murine Th epitopes including LLQYWSQELKNSAVS and is referred to as a "multideterminant region" or cluster peptide, but the longer peptide only stimulates cells from H-2^k mice				
gp160 (799–813)	gp41 (806–820 IIIB)	LLQYWSQELKNSAVS	Vaccine	murine (H-2^{k,d,t4})	Hale1989
	Vaccine *Strain:* IIIB *HIV component:* gp160 • Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (799–813)	gp41 (806–820 IIIB)	LLQYWSQELKNSAVS	Vaccine	murine (H-$2^{k,d,t4}$)	Hale1989
	Vaccine *Strain:* IIIB *HIV component:* gp160				
	• Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types				
gp160 (814–829)	gp41 (IIIB)	WLNATAIAVTEGTDRC	in vitro stimulation	human	Manca1995b
	• Peptide stimulation of PBMC from non-infected individuals in vitro				
	• Peptide priming does not always induce T-cells that recognize whole protein				
gp160 (821–835)	gp160 (828–842 IIIB)	AVAEGTDRVIEVVQG	Vaccine	murine (H-2^k, H-2^b, H-2^s)	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Adjuvant:* Freund's adjuvant				
	• This peptide elicited proliferative responses in cells from B10.BR mice (H-$2A^k$, E^k), B10.A(5R) mice (H-$2A^b$, E^b), and B10.S(9R) mice (H-$2A^s$, E^s)				
	• AVAEGTDRVIEVVQGAYRAIRHIPRRIRQGLER encompasses several murine Th epitopes including AVAEGTDRVIEVVQG and is referred to as a "multideterminant region" or cluster peptide				
gp160 (821–835)	gp41 (828–842 IIIB)	AVAEGTDRVIEVVQG	Vaccine	murine (H-2^k)	Hale1989
	Vaccine *Strain:* IIIB *HIV component:* gp160				
	• Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types				
gp160 (821–838)	gp41 (827–843)	YVAEGTDRVIEVVQGACR	HIV-1 infection	human	Caruso1997
	• As HIV-1-infected individuals progress to disease, T-cells show reduced ability to proliferate in response to HIV antigen, but retain the ability to express the activation antigens CD25 and CD71				
	• The ability to express activation markers in response to HIV is retained, but the response to tetanus toxoid recall antigen is lost				
	• This study investigated CD25 and CD71 expression in PBMC from patients at various stages of progression, measuring the response to in vitro stimulation by peptide cocktail containing four antigenic Env peptides, or p17 and p24				
gp160 (821–853)	gp160 (828–860 IIIB)	AVAEGTDRVIEVVQGAYRA-IRHIPRRIRQGLER	HIV-1 infection, Vaccine	human, murine (H-2^k, H-2^b, H-2^s, H-2^d)	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Adjuvant:* Freund's adjuvant				
	• AVAEGTDRVIEVVQGAYRAIRHIPRRIRQGLER encompasses several murine Th epitopes and is referred to as a "multideterminant region" or cluster peptide				
	• Six multideterminant region cluster peptides were evaluated for Th responses in different MHC/HLA backgrounds after vaccination of mice with gp160, or in infected people				
	• This cluster peptide elicited proliferative responses in cells from all four MHC types tested: B10.BR mice (H-$2A^k$, E^k), B10.D2 mice (H-$2A^d$, E^d), B10.A(5R) mice (H-$2A^b$, E^b), and B10.S(9R) mice (H-$2A^s$, E^s)				
	• IL-2 production in response to this peptide was observed in only 8% (1/12) of asymptomatic HIV-infected individuals				
gp160 (827–835)	gp41 (834–842 IIIB)	DRVIEVVQG	Vaccine	murine (H-2^k)	Hale1989
	Vaccine *Strain:* IIIB *HIV component:* gp160				
	• Suggested H-2^k epitope based on region of overlap				
gp160 (827–841)	gp41 (834–848 IIIB)	DRVIEVVQGAYRAIR	Vaccine	Rhesus macaque	Hosmalin1991
	Vaccine *Vector/Type:* peptide prime with protein boost *Strain:* IIIB *HIV component:* gp160				
	• Epitope name: TH4				
	• Peptide priming to induce T-cell help enhances antibody response to gp160 immunization				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Called Th4.1 and TH4				
gp160 (827–841)	gp41 (834–848 IIIB) • Epitope name: TH4 • used in a study of the influence of pentoxifylline on HIV specific T-cells	DRVIEVVQGAYRAIR	HIV-1 infection	human	Clerici1997
gp160 (827–841)	gp41 (834–848 IIIB) • Epitope name: TH4 • CTL activity analyzed in parallel with Th reactivity in exposed but uninfected health care workers • Called Th4.1 and TH4	DRVIEVVQGAYRAIR		human	Pinto1995
gp160 (827–841)	gp41 (834–848 IIIB) • Epitope name: TH4 • Peptides stimulate Th cell function and CTL activity in similar patient populations • Called Th4.1 and TH4	DRVIEVVQGAYRAIR	HIV-1 infection	human	Clerici1991a
gp160 (827–841)	gp41 (834–848 IIIB) **Vaccine** *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 • Epitope name: TH4 • Immunizing uninfected individuals with rgp160 results in stronger Th response than does natural infection • Called Th4.1 and TH4	DRVIEVVQGAYRAIR	Vaccine	human	Clerici1991b
gp160 (827–841)	gp41 (834–848 IIIB) • Epitope name: TH4 • Cell-mediated immune response to HIV-1 peptides in HIV-1 exposed seronegative men • Called Th4.1 and TH4	DRVIEVVQGAYRAIR		human	Clerici1992
gp160 (827–841)	gp41 (834–848 IIIB) • Epitope name: TH4 • IL-2 production detection of Th lymphocytes from asymptomatic HIV-positive individuals • Called Th4.1 and TH4	DRVIEVVQGAYRAIR	HIV-1 infection	human	Clerici1989
gp160 (827–841)	gp41 (834–848 IIIB) • Epitope name: TH4 • Kenyan sex workers that remained seronegative were found to frequently have HIV-env peptide specific Th responses detected by an IL-2 assay (11/20 cases) and mucosal genital tract anti-HIV IgA (16/21 cases) • Helper epitopes used in this study were noted to be previously described [Clerici1989], and were not explicitly described in [Kaul1999]	DRVIEVVQGAYRAIR	HIV-1 infection	human	Kaul1999
gp160 (827–841)	gp41 • Epitope name: TH4, Th4.1 • In a S. African perinatal transmission study, 33% (33/86) of cord blood samples from infants with seropositive mothers produced T-helper responses (measured by a bioassay measuring IL2 production in a murine cell line and confirmed with a proliferation assay) against a peptide cocktail containing Th epitopes P18 MN, P18 IIIB, T1, T2, and TH4 • The mothers were predominantly infected with subtype C, but the T help response was detectable in a number of cord blood samples despite using peptides based on B subtype reagents.	DRVIEVVQGAYRAIR	HIV-1 infection, HIV-1 exposed seronegative	human	Kuhn2001

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• 3/33 infants with cord blood T help responses to Env were infected *in utero*, 2/33 were lost to follow up, and 28/33 were not infected. 6/53 of the infants with cord blood that was unresponsive to Env peptide stimulation were infected before delivery, and 8/47 contracted HIV intrapartum or via breast-feeding. • Measurable HIV specific T help responses elicited in the immunologically immature newborn, possibly in response to *in utero* exposure, are associated with a protective natural immunity that helps block mother-infant transmission of HIV-1.				
gp160 (827–841)	gp160 (834–848 IIIB)	DRVIEVVQGAYRAIR	Vaccine	murine (H-2^k, H-2^b)	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Adjuvant:* Freund's adjuvant • This peptide elicited proliferative responses in cells from B10.BR mice (H-2A^k, E^k) and B10.A(5R) mice (H-2A^b, E^b)				
gp160 (827–841)	gp41 (834–848 IIIB) **Vaccine** *Strain:* IIIB *HIV component:* gp160 • Epitope name: TH4 • Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types • Called Th4.1 and TH4	DRVIEVVQGAYRAIR	Vaccine	murine (H-$2^{k,i5}$)	Hale1989
gp160 (829–843)	gp160 (836–850 IIIB)	VIEVVQGAYRAIRHI	Vaccine	murine (H-2^k, H-2^b)	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Adjuvant:* Freund's adjuvant • This peptide elicited proliferative responses in cells from B10.BR mice (H-2A^k, E^k) and B10.A(5R) mice (H-2A^b, E^b)				
gp160 (834–841)	gp41 (841–848 IIIB) **Vaccine** *Strain:* IIIB *HIV component:* gp160 • Suggested H-2^k epitope based on region of overlap	QGAYRAIR	Vaccine	murine (H-2^{i5})	Hale1989
gp160 (834–848)	gp160 (841–855 IIIB)	QGAYRAIRHIPRRIR	Vaccine	murine (H-2^k, H-2^b, H-2^d, H-2^s)	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Adjuvant:* Freund's adjuvant • This peptide elicited proliferative responses in cells from B10.BR mice (H-2A^k, E^k), B10.A(5R) mice (H-2A^b, E^b), B10.D2(H-2A^d, E^d), and B10.S(9R) mice (H-2A^s, E^s)				
gp160 (834–848)	gp41 (841–855 IIIB) **Vaccine** *Strain:* IIIB *HIV component:* gp160 • Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types	QGAYRAIRHIPRRIR	Vaccine	murine (H-$2^{d,t4,i5}$)	Hale1989
gp160 (839–848)	gp41 (846–855 IIIB) **Vaccine** *Strain:* IIIB *HIV component:* gp160 • Suggested H-$2^{d,t4}$ epitope based on region of overlap	AIRHIPRRIR	Vaccine	murine (H-$2^{d,t4}$)	Hale1989
gp160 (839–853)	gp160 (828–842 IIIB)	AIRHIPRRIRQGLER	Vaccine	human, murine (H-2^k, H-2^b, H-2^s)	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 *Adjuvant:* Freund's adjuvant • This peptide elicited proliferative responses in cells from B10.BR mice (H-2A^k, E^k), B10.A(5R) mice (H-2A^b, E^b), and B10.S(9R) mice (H-2A^s, E^s)				
gp160 (839–853)	gp41 (846–860 IIIB) **Vaccine** *Strain:* IIIB *HIV component:* gp160	AIRHIPRRIRQGLER	Vaccine	murine (H-$2^{d,t4}$)	Hale1989

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types				
gp160 (842–856)	gp41 (842–856 IIIB, B10) • 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.	HIPRRIRQGLERILL	HIV-1 infection	human	Wahren1989b, Wahren1989a
gp160	gp120 (IIIB) • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 4/15 responders recognized this peptide, average SI = 4.4.		HIV-1 infection	human	Geretti1994
gp160	gp120 (IIIB) • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 4/15 responders recognized this peptide, average SI = 4.4.		HIV-1 infection	human	Geretti1994

III-B-15 Env Helper T-Cell Epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Env	gp120 (IIIB)		Vaccine	murine	Shiver1997
	Vaccine *Vector/Type:* DNA *Strain:* IIIB *HIV component:* gp120, gp160				
	• DNA vaccinations of BALBc mice with a gp120 or gp160 DNA vaccine elicited a strong T-cell proliferative response with Th1-like secretion of γ interferon and IL-2, with little or no IL-4, as well as antigen specific gp120 Abs				
	• An intramuscular route of inoculation gave a stronger proliferative response than intradermal				
	• A proliferative response could be detected in all lymph tissues tested: spleen, PBMC, and mesenteric, iliac, and inguinal lymph nodes				
Env	gp120		Vaccine	murine	Kim1997d
	Vaccine *Vector/Type:* DNA *HIV component:* gp160, GAG, POL *Adjuvant:* CD86 expression vector				
	• A gp160 DNA vaccine, when delivered in conjunction with the plasmid encoding the co-stimulatory molecule CD86, gives an increase in the proliferative responses to gp120 in mice				
Env	gp120			human	De Berardinis1997
	• Sequences flanking helper T-cell immunogenic domains can be important for immunogenicity				
Env	gp120		HIV-1 infection	human	Rosenberg1997
	• A strong proliferative response to p24 and gp160 was found in a healthy long term survivor				
Env	gp120		HIV-1 infection	Macaca nemestrina	Kent1997b
	• Macaca nemestrina can be infected with HIV, and clear the infection within 6 months, so it is of interest to examine their initial immune response				
	• A strong proliferative response against gp160 with IL-4 production, indicating a Th2 response, was found with 4 weeks of infection				
	• The gp160 proliferative response by 8 weeks produces both IL-4 and γ interferon, indicating both Th1 and Th2 responses				
Env	gp120 (HXBc2)		Vaccine	Rhesus macaque	Letvin1997
	Vaccine *Vector/Type:* DNA prime with rgp160 boost *Strain:* HXBc2 *HIV component:* gp160				
	• Vaccination of Macaca mulatta (rhesus monkeys) with a HXBc2 env DNA prime and a protein boost elicited a T-cell proliferative response, a CTL response, and type-specific neutralizing antibodies				
	• Vaccinated animals challenged with SHIV-HXB2 were protected from infection				
Env	gp120 (MN)		HIV-1 infection, Vaccine	human	MacGregor1998
	Vaccine *Vector/Type:* DNA *Strain:* MN *HIV component:* ENV, REV				
	• An HIV DNA env and rev vaccine given to 15 asymptomatic HIV+ individuals at three different dosages, 30, 100 or 300 μg, was safe				
	• All three groups showed an increased proliferative response after vaccination				
Env	Env			human	Mazzoli1997
	• Study of HIV-specific immunity in seronegative partners of HIV-positive individuals – Env peptides could stimulate IL-2 production in 9/16 HIV-exposed seronegative individuals, and only 1/50 low-risk controls				
	• Exposed-uninfected produced more IL-2 and less IL-10 then HIV-infected individuals				
	• 8/9 of those whose PBMC produce IL-2 in response to Env peptides had concomitantly detected urinary or vaginal tract anti-HIV IgA				
Env	Env		HIV-1 infection	human	Plana1998
	• Patients from later stages of infection given HAART do not show restoration of HIV-1 specific Th proliferative responses				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Env	Env		HIV-1 infection	human	Kelleher1998a
	• Env and gag Th epitopes were pooled and used to test Th proliferative responses after IL2 therapy – while IL2 therapy causes an increase in CD4+ lymphocyte count, it does not increase HIV-1 specific proliferative responses				
Env	gp160		HIV-1 infection, Vaccine	human	Ratto-Kim1999
	Vaccine *Vector/Type:* recombinant protein *HIV component:* gp160				
	• Vaccinations with rgp160 did not enhance Th immunoproliferative responses in individuals who were immunized every 2 months for 5 years starting early in infection				
Env	gp160		HIV-1 infection, Vaccine	human	Leandersson2000
	Vaccine *Vector/Type:* recombinant protein *HIV component:* gp160				
	• 27 HIV subtype B, 4 subtype C, 2 D and one of each subtype E, F, G infected individuals were either given rgp160 B clade immunizations or placebo. All rgp160 immunized individuals showed increased proliferation responses to the B clade immunizing antigen rgp160.				
	• gp120 was prepared from A, B, C, D, and E subtype virions and used as antigenic stimulus – 7 of 10 tested individuals responded to native gp120 from at least one additional subtype in addition to B subtype, while a placebo recipient did not respond to any gp120				
	• This study shows that cross-subtype HIV-specific T-cell proliferative responses can be stimulated in patients already infected with another HIV-1 subtype – all immunized subjects could respond to the subtype B immunogen, but many developed responses to at least one more subtype				
Env	gp160 (MN)		Vaccine	human	Gorse1999a
	Vaccine *Vector/Type:* gp160 prime with gp120 boost *Strain:* MN *HIV component:* gp160, gp120				
	• Helper T-cell memory responses were induced by MN rgp160 as measured by proliferation and Th1 and Th2 cytokine release – this response could be boosted by MN rgp120				
Env	gp120		Vaccine	Rhesus macaque	Heeney1998b
	Vaccine *Vector/Type:* ISCOM or fowlpoxvirus *Strain:* SF2 *HIV component:* gp120				
	• Vaccinated monkeys with the highest level of Th1 and Th2 responses and the highest levels of NAbs were protected against a SHIV SF13 challenge – the ISCOM strategy gave more potent anti -gp120 responses than the Fowl pox strategy				
	• When animals were challenged 4 months after boost, those that maintained high levels of HIV-1 specific IFN-gamma responses, indicative of a Th 1 response, were still protected				
Env	(IIIB)		HIV-1 infection, Vaccine	human	Boyer1999
	Vaccine *Vector/Type:* DNA *Strain:* IIIB *HIV component:* ENV, REV				
	• A DNA vaccine containing env and rev was tested for safety and immune response in 15 HIV+ asymptomatic individuals				
	• Enhanced proliferative activity and higher levels of MIP-1 alpha were detected in multiple study subjects				
Env	Env		Vaccine	murine BALB/c	Rodríguez1999
	Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* gp160 *Adjuvant:* GM-CSF-ENV chimera				
	• A chimeric GM-CSF-env antigen expressed in a vaccinia vector elicits a higher HIV-specific env cellular immune response than when native env is used				
Env	Env (LAI)		Vaccine	Macaca nemestrina	Kent1998
	Vaccine *Vector/Type:* DNA prime with vaccinia boost *Strain:* LAI *HIV component:* ENV, GAG				
	• Priming with an HIV-DNA vaccine and boosting with a vaccinia construct induced greater levels of HIV T-cell immunity than either vaccine alone				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The proliferative response to Env and Gag after the DNA vaccination had a mean SI of 1.5-4, but after boosting with rHIV-fowlpox virus, there was a 6-17 fold increase in the mean SI for HIV Gag and Env. The T help response happened despite a fall in antibody titers, suggesting that the Th response was primarily Th1, not Th2. The CTL response was also enhanced				
Env	gp120		Vaccine	Rhesus macaque	Heeney1999
	Vaccine *Vector/Type:* DNA, protein, virus-like particle, ISCOM • Ten different vaccine strategies were evaluated for their ability to protect from infection in a rhesus macaque model using a non-pathogenic SHIV challenge. Protection correlated with the magnitude of NAb responses, beta-chemokines, and a balanced Th response. DNA, protein+adjuvant, VLP and ISCOM vaccines were tested. • HIV-1/ISCOMS gave the highest NAb titers, Th1 and Th2 responses, was the only vaccine formulation tested with a detectable CTL response, and gave enhanced beta-chemokine production.				
Env	gp160 (MN)		HIV-1 infection, Vaccine	human	Kundu1998a
	Vaccine *Vector/Type:* protein *Strain:* MN *HIV component:* gp160 • This study followed 10 HLA-A2 asymptomatic HIV+ individuals as they received MN gp160 vaccinations over a two year period. • There was an increased lymphoproliferative response but this did not impact viral load or CTL response.				
Env	gp120 (SF2)		Vaccine	Rhesus macaque	Verschoor1999
	Vaccine *Vector/Type:* DNA, recombinant protein, ISCOM *Strain:* SF2 *HIV component:* gp120 *Adjuvant:* Adjuvant MF59 • 16 rhesus Macaques were vaccinated with either an epidermal SF2 gp120 DNA vaccine, rgp120 with a MF59 adjuvant, or rgp120 incorporated into ISCOMs • DNA vaccination elicited a weak Th type 1 response and low antibody response, rgp120/MF59 triggered a strong antibody response, and rgp120/ISCOM induced both kinds of Th cells, and a strong humoral response. • Animals were challenged with SF13 SHIV. Early induction of Th type 1 and type 2 responses with the rgp120/ISCOM vaccine provided the most effective immunity, protecting from infection				
Env	Env (MN)		Vaccine	murine	Kim1998
	Vaccine *Vector/Type:* DNA *Strain:* MN *HIV component:* GAG, POL, ENV *Adjuvant:* CD80 and CD86 expression vectors • Co-stimulatory molecules co-expressed with an HIV-1 immunogen in a DNA vaccine used to enhance the immune response – co-expression of CD86, but not CD80, dramatically increased both HIV Env and Gag/Pol specific CTL and Th proliferative responses				
Env	Env (LAI, MN)		Vaccine	human	Salmon-Ceron1999
	Vaccine *Vector/Type:* canarypox *Strain:* MN, LAI *HIV component:* gp120, gp41, Gag, Protease • A live attenuated canarypox vector expressing MN gp120 and LAI gp41/gag/protease could induce CTL and a lymphoproliferative response in healthy uninfected volunteers				
Env	Env		Vaccine	Rhesus macaque	Akahata2000
	Vaccine *Vector/Type:* DNA *Strain:* ZF1 *HIV component:* complete genome • Rhesus macaques were vaccinated by i.m. injection with naked plasmid DNA carrying an HIV-1 complete genome vaccine, strain ZF1, with a mutated zinc finger in the nucleocapsid to prevent packaging • Env and Gag specific CTL but no antibody responses were induced in 2/4 vaccinated monkeys (MM145 and MM153) • 2/4 monkeys (MM146 and MM143) produced antibodies against p24 and/or gp160, but no CTL response was detected • PBMC from all vaccinated monkeys produced IFNγ, in response to HIV-1 gp160, indicating a Th response – this response was 5 times higher in MM145, the animal with the strongest CTL response				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• 4 weeks post-challenge with SHIV NM-3rN plasma viral loads of both MM145 and MM153 (with a homologous Env) decreased to near or below the detection limit • 6-8 weeks post-challenge with SHIV NM-3rN plasma viral loads of both MM146 and MM143 decreased near or below the detection limit				
Env	gp120 (W6.ID)		HIV-1 infection	human	Zhang2001b
	• T-helper cell proliferative responses to HIV p24, p55 and gp120 were tested in 27 patients with HIV infection – vigorous responses directed at Gag were detected in ten patients, but an Env specific response was detected in only one patient				
Env	gp160		HIV-1 infection	human	Blazevic2000
	• Prolonged viral suppression resulting from potent anti-retroviral therapy did not allow an HIV T helper response to p24 or gp160, but Th proliferative responses to influenza, alloantigen, and PHA did develop in many HIV+ patients, and asymptomatic patients had stronger and more frequent Th response recovery than AIDS patients				
Env	gp120		HIV-1 infection	human	Oxenius2000
	• Patients who started therapy at acute HIV infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable				
Env	gp120		Vaccine	human	Sabbaj2000
	Vaccine *Vector/Type:* canarypox prime with rgp120 boost *HIV component:* gp120 • Proliferative responses in PBMC of uninfected individuals that were vaccinated with canarypox vector expressing HIV-1 antigens (ALVAC-HIV) and boosted with a recombinant gp120 subunit vaccine gave a Th1 and Th2 proliferative response upon stimulation with HIV-1 Env • All vaccinees produced IFNγ and IL10, most also produced IL-2, IL-6, IL-4 and IL-5				
Env	gp120		HIV-1 infection, Vaccine	human	Hladik2001
	Vaccine *Vector/Type:* recombinant protein *Strain:* MN *HIV component:* gp120 *Adjuvant:* no adjuvant • 16/29 HIV-1 infected and 24/30 vaccinated individuals had DTH reactions within 48 hours after an intradermal rec gp120 injection. Of nine DTH positive individuals, none had detectable proliferative responses. Thus skin testing may be a sensitive way to identify people with Th recall responses to vaccines, or in the absence of lymphoproliferaion. • No 48 hour DTH responses were detected among uninfected volunteers, although 10/35 (40%) of the high risk and 11/32 (34%) of the low risk individuals developed an induration resembling DTH after 7-12 days, that may be indicative of primary induction of HIV-1 specific Th1-immunity.				
Env	gp120		HIV-1 infection	human	Wilson2000b
	• Dysfunction of HIV-1 specific proliferative responses, but not responses to other antigens, is evident in HIV-1 progressive disease. • Vigorous HIV-1 specific responses to p24, Nef and gp120 with SI between 8-99 were seen in 6/7 long term non-progressors (LTNP), the seventh had a borderline responses. IL-2 production was seen in all cases, and IL-4 production was also evident many responses. • None of the progressors (0/5) had HIV-1 specific proliferative responses, or IL-2 or IL-4 induction. • Non-HIV antigens (cytomegalovirus, PPD, Staphylococcus enterotoxin B, tetanus toxoid) gave similar responses in HIV-1+ LTNP, progressors, and HIV-1 controls.				
Env	gp160		HIV-1 infection	human	Kalams1999a
	• The strength of p24 specific Gag proliferative responses (SIs) were inversely correlated with viral load in 21 ARV naive patients. The responses were Th1, IFNgamma producing. • Proliferative responses against gp160 were rarely observed (only 4 cases).				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Env	Env		Vaccine	human	MacGregor2002
	Vaccine *Vector/Type:* DNA with CMV promotor *Strain:* MN *HIV component:* Env, Rev *Adjuvant:* bupivacaine				
	• A phase I clinical trial of a HIV-1 Env and Rev DNA vaccine with a CMV promoter was conducted and Th proliferative, CTL and Elispot responses monitored. The construct was modified for safety and included no LTRs or packaging signals. The vaccine strategy was safe, and elicited strong CD4-T cell responses, but not CD8 T-cell responses. Rev elicited strong Th responses, and is a early produced protein so may confer advantages.				
	• With a 300 ug dose, 4/6 individuals had a lymphocyte proliferation (LP) responses to gp120, 3/6 to Rev.				
	• With a 1000 ug dose, 4/6 individuals had a LP and 2/6 had IFNgamma Elispot responses to gp160; 3/6 had LP, and 4/6 had IFNgamma Elispot responses to Rev.				
	• No responses to three specific CTL epitopes were observed by Elispot in individuals with appropriate HLA. Some cytoxic activity against whole protein was observed that was CD4+ T-cell mediated.				
Env			HIV-1 infection	human	Clerici2002b
	• Specific immunity was compared in a two-year study of chronically HIV-1 infected i) HAART-naive patients who were not progressing and had strong immune responses, ii) newly treated patients followed for 24 months after initiation of HAART, iii) and long-term HAART patients who had been on HAART at least 12 months prior to the study.				
	• HAART naïve patients had strongest proliferative responses at time zero, but long-term HAART patients the most significant increase in specific responses over the two year study period against HIV-1 gp160, influenza, and Candida. Similarly, IL-2 and IFNγ production in responses to gp160 was highest in the naïve group at time zero, but increased the most in the long-term HAART treated patients.				
	• Short-term HAART patients showed a significant improvement in their CD4+ T cell count and a reduction of plasma viremia, and had augmented IL-7 production, which was slightly reduced in long-term HAART patients.				
Env	gp160		HIV-1 infection	human	Palmer2002
	• CD4+ T cell proliferative responses from 33 HIV-1 infected patients with HAART suppression were compared to 19 patients with active viral replication (HAART failures and HAART naive). Patients with HAART suppression showed stronger p24- and p66-specific proliferative responses compared to patient groups with active HIV-1 replication, suggesting active viral replication in vivo specifically reduces proliferation responses.				
	• gp160 proliferation responses were apparent in 7/32 donors tested, but weaker overall, with a median value for the suppressed group not above that found for HIV seronegative controls.				
	• No differences in the frequency of HIV-specific CD4+ T-cells that were positive for cytokine secretion in a flow cytometry assay were found in the HAART suppressed group versus the group with active viral replication.				
Env	gp120 (SF2)		HIV-1 infection	human	Imami2002b
	• 70 patients with chronic disease progression, 10 clinical non-progressors, and 3 immunologically discordant progressors (individuals who controlled viremia but had progressive CD4+ T-cell decline) were analyzed for their T-helper cell responses to p24 and cytokine profile.				
	• In a comparison of responses to HIV-1 proteins based on 10 non-progressors, 3 immunologically discordant, and 70 progressors, SIs were always much higher for non-progressors and immunologically discordant than progressors. Among the non-progressors, the responses to different antigens were greater using p24 peptides than native p24. Native p24, Nef, gp120 proteins, and Remune (gp120 depleted HIV-1, p24 is subtype G), had roughly comparable distributions of SI values from the non-progressors, Nef and gp120 responses were somewhat diminished in immunologically discordant patients.				
Env	(BRU)		Vaccine	murine	Haas1991
	Vaccine *Vector/Type:* inactivated virus *Strain:* BRU *HIV component:* whole virus *Adjuvant:* Complete Freund's adjuvant (CFA)				
	• Of 5 mouse inbred lines tested: DBA/2 (H-2d, Ad, Ed), B10.A(4R) (H-2h4, Ak) and B10.A(5R) (H-2i5) showed particularly good CD4+ T cell proliferative responses to HIV proteins (gp160, gp120, p17, p24, Nef and RT), after vaccination with inactivated virus.				
	• B10.BR (H-2k, Ak, Ek) and C57BL/6 (H-2b and Ab) had weaker responses.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Env	gp120		Vaccine	murine (H-2^d)	Kim2000
	Vaccine *Vector/Type:* DNA *HIV component:* GAG, POL, ENV *Adjuvant:* IL-2, IL-4 and IFNγ expression vectors				
	• Co-stimulatory molecules co-expressed with an HIV-1 immunogen in a DNA vaccine used to enhance the immune response – co-expression of Th1 cytokine IFN-gamma drove Th1 immune responses and enhanced CTL responses				
Env	gp120 (IIIB)		Vaccine	murine (H-2^d)	Shirai2001
	Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* gp160				
	• Helicobacter pylori induces Th1 responses early, but predominantly Th2 responses later in infection (at 6 weeks) – differentiation of HIV-1 gp160 CD4+ help and CD8+ CTL effector cells in response to HIV gp160-vaccinia vaccination is impaired in BALB/c mice infected with H. pylori				
Env	gp120 (V3) and p24 (IIIB, MN, BH10)		Vaccine	murine (H-2^d)	Buonaguro2002
	Vaccine *Vector/Type:* virus-like particle *Strain:* gp120 A clade UG5.94UG018, HIV-1 IIIB *HIV component:* gp120 and Pr55gag				
	• BALB/c mice were given intraperitoneal immunization in the absence of adjuvants with virus-like particles (VLPs) expressing recombinant subtype A gp120 and Pr55gag				
	• High dose-independent humoral responses were elicited against both gp120 and p24 peptides, and CTL responses were observed against target cells carrying vaccinia expressed gp120 and Gag.				
	• Recombinant rgp120 (clade B, MN) induced T cell proliferative responses in vitro from vaccinated animals.				
Env	gp160 (IIIB)		Vaccine	murine ($H2^d$)	Morris2000
	Vaccine *Vector/Type:* peptide, recombinant protein *Strain:* IIIB *HIV component:* gp160, V3 *Adjuvant:* Adjuvant LT(R192G)				
	• Mice were intranasally immunized with 20 ug of HIV-gp160 and 5 ug of peptide E7 (RIHIGPGRAFYAARK) with the adjuvant LT(R192G), a heat-labile enterotoxin produced by E. coli				
	• Adjuvant LT(R192G) was required for stimulation of antigen-specific IgG1, IgG2 antibodies, and Th1 and Th2 cytokines responses to gp160, and peptide-specific CTL responses				
	• Increased IFN-gamma, IL-10 and IL-6 cytokine production specific to gp160 was measured with co-immunization of gp160 with LT(R192G)				
Env	gp160 (IIIB)		Vaccine	murine ($H2^d$)	Arai2000
	Vaccine *Vector/Type:* DNA with CMV promotor *Strain:* IIIB *HIV component:* gp160, REV *Adjuvant:* Br-cAMP				
	• The CMV promotor responds to the intracellular level of cAMP, and 8 Br-cAMP can increase transgene expression so it was co-administered with a CMV-based DNA vaccine both intranasally and intramuscularly				
	• 8 Br-cAMP increased serum IgG responses, HIV-specific CTL, DTH and Th1 responses, and IgA in the intranasal vaccination				
	• A CAT assay study showed adjuvant effect was due to CMV promotor activation				

III-B-16 Nef Helper T-Cell Epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (1–20)	Nef (1–20 LAI)	MGGKWSKSSVVGWPTVRERM	Vaccine	murine (H-2^d)	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* LAI *HIV component:* NEF, TAT, REV • Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein • Proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev				
Nef (1–20)	Nef (1–20 HXB2)	MGGKWSKSSVIGWPTVRERM	HIV-1 infection	(H-2^d)	Peng2001
	• Deletion of the 19 N-terminal amino acids from Nef including the myristolation signal eliminates Nef-induced down-regulation of MHC class I and CD4 molecules. Such a construct has the potential to serve as a more potent immunogen. The known T-cell epitopes that that would be disputed by this deletion are minimal, a murine H-2d Th epitope in the peptide MGGKWSKSSVIGWPTVRERM, and a HLA-B8 CTL epitope, WPTVRERM.				
Nef (16–35)	Nef (16–35 LAI)	VRERMRRAEPAADGVGAASR	Vaccine	murine (H-2^d)	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* LAI *HIV component:* NEF, TAT, REV • Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein • Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev				
Nef (31–50)	Nef (31–50 LAI)	GAASRDLEKHGAITSSNTAA	Vaccine	murine (H-2^d)	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* LAI *HIV component:* NEF, TAT, REV • Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein • Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev				
Nef (45–69)	Nef (45–69 BRU)	SSNTAATNAACAWLEAQEE-EEVGFP	Vaccine	chimpanzee, rat	Estaquier1992
	Vaccine *Vector/Type:* peptide prime with protein boost *Strain:* BRU *HIV component:* Nef • Antigenic domain: ATNAACAWL, priming with peptide enhanced subsequent Ab response to Nef protein immunization				
Nef (45–69)	Nef (45–69)	SSNTAATNAACAWLEAQEE-EEVGFP	Vaccine	rat	Rouaix1994
	Vaccine *Vector/Type:* peptide *Adjuvant:* no adjuvant, aluminum hydroxide • Covalently linking the potent Th epitope Nef 45-69, which can induce Th proliferative responses at low doses with no adjuvant in Lou/M rats, to a weaker epitope from Schistosoma mansoni allows the induction of detectable Th responses to the Schistosoma epitope.				
Nef (46–65)	Nef (46–65 LAI)	SNTAATNAACAWLEAQEEEE	Vaccine	murine (H-2^d)	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* LAI *HIV component:* NEF, TAT, REV • Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein • Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev				
Nef (56–68)	Nef (56–68 HXB2)	AWLEAQEEEEVGF	Vaccine	murine (DQ2, DQ3, DQ5, DQ6, DQ7, DQ8,)	Pancré2002
	Vaccine *Vector/Type:* peptide *HIV component:* Nef *Adjuvant:* CFA • This highly conserved Nef epitope has promiscuous HLA-DQ class II binding potential. It has a can bind to 6 different HLA-DQ alleles, but did not bind to any HLA-DR alleles tested. It bound to DQ2 and DQ8 with particularly high affinity, and with DQ7 with low affinity. • DQ transgenic mice (in particular DQ8) mounted strong cellular and humoral responses after immunization with this peptide.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Ex vivo stimulation of CD4+ T-cells from 14 healthy donors (with diverse HLAs) with this peptide presented on autologous DCs resulted in Th1-associated cytokine production. IFNgamma production was stimulated in 7/14 cases, both IFNgamma and IL-2 in 6/14, and just IL-2 in 1/14. No IL-4 or IL-5 production was observed. • Peptide-specific CD4+ T-cell clones with different HLA presenting molecules demonstrated a preference for TCR Vbeta6.1.				
Nef (61–80)	Nef (61–80 LAI)	QEEEEVGFPVTPQVPLRPMT	Vaccine	murine (H-2^b)	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* LAI *HIV component:* NEF, TAT, REV • Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein • Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev				
Nef (66–97)	Nef (66–97 LAI)	VGFPVTPQVPLRPMTYKAA-VDLSHFLKEKGGL	Vaccine	human	Gahery-Segard2000
	Vaccine *Vector/Type:* lipopeptide • Anti-HIV lipopeptide vaccine consisting of six long peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial • A CD4+ T cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 5/10 reacted to this Nef peptide • 9/12 tested mounted a CTL responses to at least one of the six peptides, each of the six peptides elicited a CTL response in at least one individual • 5/12 tested had an IgG response to this peptide				
Nef (76–95)	Nef (76–95 LAI)	LRPMTYKAAVDLSHFLKEKG	Vaccine	murine (H-2^b)	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* LAI *HIV component:* NEF, TAT, REV • Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein • Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev				
Nef (91–110)	Nef (91–110 LAI)	LKEKGGLEGLIHSQRRQDIL	Vaccine	murine (H-2^b)	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* LAI *HIV component:* NEF, TAT, REV • Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein • Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev				
Nef (98–112)	Nef (98–112 BRU)	EGLIHSQRRQDILDL	Vaccine	chimpanzee	Estaquier1992
	Vaccine *Vector/Type:* peptide prime with protein boost *Strain:* BRU *HIV component:* Nef • Peptide alone could stimulate monkey T-cells in the absence of carrier protein – required carrier protein in rat				
Nef (104–123)	Nef (106–125 HXB3)	QRRQDILDLWIYHTQGYFP-D?	Vaccine	murine (H-2^b)	Sandberg2000
	Vaccine *Vector/Type:* DNA *Strain:* HXB3 *HIV component:* Nef • A strong T helper proliferative response against a rec Nef protein was observed 2 weeks after immunization of HLA-A201 transgenic mice in a C57Bl/6 background – the response was weak by 4 weeks post immunization • Mice were immunized with nef DNA under the control of a CMV promotor, coated on gold particles delivered to abdominal skin by a gene gun • Primary responses were directed at peptides 106-125, 166-185, and 181-205, indicating a response to multiple epitopes				
Nef (106–125)	Nef (106–125 LAI)	RQDILDLWIYHTQGYFPDWQ	Vaccine	murine (H-2^b)	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* LAI *HIV component:* NEF, TAT, REV • Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein • Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (117–147)	Nef (117–147 LAI)	TQGYFPDWQNYTPGPGVRY-PLTFGWCYKLVP	Vaccine	human	Gahery-Segard2000
	Vaccine *Vector/Type:* lipopeptide • Anti-HIV lipopeptide vaccine consisting of six long peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial • A CD4+ T cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 1/10 reacted to this Nef peptide • 9/12 tested mounted a CTL responses to at least one of the six peptides, each of the six peptides elicited a CTL response in at least one individual • 10/12 tested had an IgG response to this peptide				
Nef (121–140)	Nef (121–140 LAI)	FPDWQNYTPGPGVRYPLTFG	Vaccine	murine (H-2^b)	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* LAI *HIV component:* NEF, TAT, REV • Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein • Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev				
Nef (136–155)	Nef (136–155 LAI)	PLTFGWCYKLVPVEPDKVEE	Vaccine	murine (H-2^d)	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* LAI *HIV component:* NEF, TAT, REV • Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein • Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev				
Nef (151–170)	Nef (151–170 LAI)	DKVEEANKGENTSLLHPVSL	Vaccine	murine (H-2^d)	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* LAI *HIV component:* NEF, TAT, REV • Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein • Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev				
Nef (164–183)	Nef (166–185 HXB3)	LLHPVSLHGMDDPEREVLE-W?	Vaccine	murine (H-2^b)	Sandberg2000
	Vaccine *Vector/Type:* DNA *Strain:* HXB3 *HIV component:* Nef • A strong T helper proliferative response against a rec Nef protein was observed 2 weeks after immunization of HLA-A201 transgenic mice in a C57Bl/6 background – the response was weak by 4 weeks post immunization • Mice were immunized with nef DNA under the control of a CMV promotor, coated on gold particles delivered to abdominal skin by a gene gun • Primary responses were directed at peptides 106-125, 166-185, and 181-205, indicating a response to multiple epitopes				
Nef (166–185)	Nef (166–185 LAI)	HPVSLHGMDDPEREVLEWRF	Vaccine	murine (H-$2^{b,d}$)	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* LAI *HIV component:* NEF, TAT, REV • Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein • Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev				
Nef (179–198)	Nef (181–205 HXB3)	EVLEWRFDSRLAFHHVARE-L?	Vaccine	murine (H-2^b)	Sandberg2000
	Vaccine *Vector/Type:* DNA *Strain:* HXB3 *HIV component:* Nef • A strong T helper proliferative response against a rec Nef protein was observed 2 weeks after immunization of HLA-A201 transgenic mice in a C57Bl/6 background – the response was weak by 4 weeks post immunization • Mice were immunized with nef DNA under the control of a CMV promotor, coated on gold particles delivered to abdominal skin by a gene gun • Primary responses were directed at peptides 106-125, 166-185, and 181-205, indicating a response to multiple epitopes				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (181–205)	Nef (181–205 LAI)	LEWRFDSRLAFHHVARELH-PEYFKN	Vaccine	murine (H-2^d)	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* LAI *HIV component:* NEF, TAT, REV				
	• Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein				
	• Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev				
Nef (182–205)	Nef (182–205 LAI)	EWRFDSRLAFHHVARELHP-EYFKN	Vaccine	human	Gahery-Segard2000
	Vaccine *Vector/Type:* lipopeptide				
	• Anti-HIV lipopeptide vaccine consisting of six long peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial				
	• A CD4+ T cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 4/10 reacted to this Nef peptide				
	• 9/12 tested mounted a CTL responses to at least one of the six peptides, each of the six peptides elicited a CTL response in at least one individual				
	• None of the 12 tested had an IgG response to this peptide				
Nef (185–200)	Nef (183–198)	FDSRLAFHHVARELHP	HIV-1 infection	human	Ranki1997
	• T-cell response to this epitope persisted after seroreversion				
Nef (186–206)	Nef(p27) (185–205 BRU)	DSRLAFHHVARELHPEYFK-NC	Vaccine	chimpanzee	Bahraoui1990
	Vaccine *Vector/Type:* recombinant protein *Strain:* BRU *HIV component:* gp160, p25, Nef, p17 and p24 Gag *Adjuvant:* muramyl-dipeptide base adjuvant (Syntex)				
	• Epitope name: PF63				
	• Six chimpanzees were immunized with rec vaccinia viruses (VV) expressing HIV-1 gp160, Gag, and Nef.				
	• 2/6 chimpanzees showed persistent T-helper proliferative responses against a putative immunodominant epitope located at the C-term end of Nef.				
Nef	Nef (LAI)		HIV-1 infection	human	daSilva1998
	• This study compares the level of variation in Nef CTL epitopes to helper and MAb epitopes from the same region				
	• CTL epitopes tend to be more conserved than either helper or MAb epitopes and there are stronger functional constraints in the regions where CTL epitopes cluster.				
Nef	Nef		Vaccine	human	Calarota1999
	Vaccine *Vector/Type:* DNA *HIV component:* Nef, Rev Tat				
	• 9/9 HIV-1+ subjects were given one of three DNA vaccinations for nef, rev or tat, and novel proliferative and CTL responses were generated				
	• The nef DNA immunization induced the highest and most consistent CTLp activity, IFN-gamma production, and IL-6 and IgG responses				
	• Highly active antiretroviral treatment (HAART) did not induce new HIV-specific CTL responses but reduced viral load, while DNA vaccination induced new immune responses but did not reduce viral load – thus this is a potentially complementary and promising combination				
Nef	Nef		HIV-1 infection, Vaccine	human	Calarota2001
	Vaccine *Vector/Type:* DNA *HIV component:* Nef, Rev, Tat *Adjuvant:* CpG motifs				
	• This review discusses the cellular immune response, and comments on CpG induction of Th1 cytokines and enhanced immune responses, and HIV-1 DNA vaccine boosting of CTL and Th proliferative responses in asymptomatic HIV+ individuals				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef	Nef		HIV-1 infection	human	Oxenius2000
	• Patients who started therapy at acute HIV infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable				
Nef	Nef		HIV-1 infection	human	Wilson2000b
	• Dysfunction of HIV-1 specific proliferative responses, but not responses to other antigens, is evident in HIV-1 progressive disease. • Vigorous HIV-1 specific responses to p24, Nef and gp120 with SI between 8-99 were seen in 6/7 long term non-progressors (LTNP), the seventh had a borderline responses. IL-2 production was seen in all cases, and IL-4 production was also evident many responses. • None of the progressors (0/5) had HIV-1 specific proliferative responses, or IL-2 or IL-4 induction. • Non-HIV antigens (cytomegalovirus, PPD, Staphylococcus enterotoxin B, tetanus toxoid) gave similar responses in HIV-1+ LTNP, progressors, and HIV-1 controls.				
Nef	Nef (BRU)		Vaccine	murine	Moureau2002
	Vaccine *Vector/Type:* recombinant protein *Strain:* BRU *HIV component:* Nef *Adjuvant:* poly(DL-lactide-co-glycolide) (PLG), Freund's adjuvant • BALB/c mice were immunized with Nef alone, Nef with Freund's adjuvant, or Nef encapsulated in poly(DL-lactide-co-glycolide) PLG microparticles. • High Ab titers (predominantly IgG1) against Nef were retained for seven months in the mice infected with Nef-PLG, 3-fold higher than Nef in Freund's, 5-fold higher than Nef alone. • CD4+ T-cell lymphoproliferative were observed, and cytokine profiles indicated this was primarily a Th2 response.				
Nef	Nef (SF2)		HIV-1 infection	human	Imami2002b
	• 70 patients with chronic disease progression, 10 clinical non-progressors, and 3 immunologically discordant progressors (individuals who controlled viremia but had progressive CD4+ T-cell decline) were analyzed for their T-helper cell responses to p24 and cytokine profile. • In a comparison of responses to HIV-1 proteins based on 10 non-progressors, 3 immunologically discordant, and 70 progressors, SIs were always much higher for non-progressors and immunologically discordant than progressors. Among the non-progressors, the responses to different antigens were greater using p24 peptides than native p24. Native p24, Nef, gp120 proteins, and Remune (gp120 depleted HIV-1, p24 is subtype G), had roughly comparable distributions of SI values from the non-progressors, Nef and gp120 responses were somewhat diminished in immunologically discordant patients.				
Nef	(BRU)		Vaccine	murine	Haas1991
	Vaccine *Vector/Type:* inactivated virus *Strain:* BRU *HIV component:* whole virus, RT *Adjuvant:* Complete Freund's adjuvant (CFA) • Of 5 mouse inbred lines tested: DBA/2 (H-2d, Ad, Ed), B10.A(4R) (H-2h4, Ak) and B10.A(5R) (H-2i5) showed particularly good CD4+ T cell proliferative responses to HIV proteins (gp160, gp120, p17, p24, Nef and RT), after vaccination with inactivated virus. • B10.BR (H-2k, Ak, Ek) and C57BL/6 (H-2b and Ab) had weaker responses.				
Nef	Nef		Vaccine	murine (H-2^d)	Ayyavoo2000
	Vaccine *Vector/Type:* DNA *HIV component:* Vif, Vpu, Nef • Splenocytes from BALB/c mice immunized with pVVN-P DNA were incubated with Vif, Vpu or Nef antigens for 3 days and assayed for IL-4 and IFN-gamma levels • Antigen stimulation increased IFN-gamma production in pVVN-P immunized mice, indicating a Th1 response • IL-4 production was not significantly changed after antigen stimulation compared to control levels • Cross-clade CTL activity was also observed: A, B clade, CRF01(AE) clade antigens could serve as targets for the B clade immunization stimulated CTL – an HIV-1 AC recombinant, however, did not stimulate a CTL response, but was expressed at lower levels on the target cell				

III-B-17 HIV-1 Helper T-Cell Epitopes

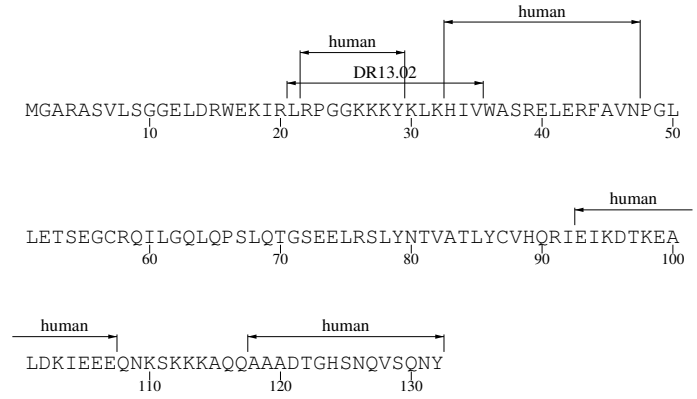
HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
HIV-1			HIV-1 infection	human	Kuhn2002
• Intrauterine exposure of infants to HIV from their mothers results in HIV-1 specific T-helper cell proliferative responses in 1/3 of exposed uninfected babies, and HIV-1 specific CTL in some. It is unknown whether these responses are associated with lack of infection, but there is some evidence that HIV-1 T-cell responses may reduce transmission in breastfeeding mothers. Summary tables are provided of CD4 and CD8 T-cell responses detected in earlier studies.					
HIV-1			HIV-1 infection, Vaccine	human	Kahn2000
Vaccine *Vector/Type:* gp120 depleted virus HZ321 (REMUNE(TM)) *Strain:* Z321 *HIV component:* gp120-depleted HIV-1 antigen *Adjuvant:* Incomplete Freund adjuvant (IFA)					
• No benefit was observed in terms of progression free survival for HIV-1 patients on ART given vaccinations with HIV-1 antigen (N=1,262) versus those vaccinated with placebo (N=1,265). There was no statistically different outcome in HIV RNA, CD4 percentage, or body weight. HIV-1 ART patients that were vaccinated did have higher absolute CD4 counts.					
HIV-1			HIV-1 infection, Vaccine	human	Moss1999
Vaccine *Vector/Type:* gp120 depleted virus HZ321 (REMUNE(TM)) *Strain:* Z321 *HIV component:* gp120-depleted HIV-1 antigen *Adjuvant:* Incomplete Freund adjuvant (IFA)					
• 15 HIV-1+ patients on ARV given vaccinations with HIV-1 antigen versus vaccinated with placebo. Lymphocyte proliferation of CD4+, CD8+ memory cells and NK cells to p24 and Remune HIV-1 antigen increased in HAART treated patients after vaccination.					
HIV-1			HIV-1 infection, Vaccine	human	Moss1997
Vaccine *Vector/Type:* gp120 depleted virus HZ321 (REMUNE(TM)) *Strain:* Z321 *HIV component:* gp120-depleted HIV-1 antigen *Adjuvant:* Incomplete Freund adjuvant (IFA)					
• HIV-1 specific stimulation of T-cell proliferation, and beta-chemokines (RANTES) and Th1-type cytokine (IFNgamma) production are found after immunization of HIV-1+ individuals with HIV-1 immunogen.					
HIV-1			HIV-1 infection, Vaccine	human	Levine1996
Vaccine *Vector/Type:* gp120 depleted virus HZ321 (REMUNE(TM)) *Strain:* Z321 *HIV component:* gp120-depleted HIV-1 antigen *Adjuvant:* Incomplete Freund adjuvant (IFA)					
• Long-term follow up of HIV-1+ individuals given HIV-1 immunogen, suggesting those patients who became HIV-DTH-responsive in response to the HIV-1 immunogen had a better clinical outcome. Of twelve who developed DTH-responsiveness, one got an opportunistic infection and died, and one developed KS. Of the 13 patients who remained HIV-DTH-nonresponsive, 9 (69%) progressed to AIDS and 7 of these had died.					
HIV-1			Vaccine	human	Turner1994
Vaccine *Vector/Type:* HIV-1 immunogen *Adjuvant:* Incomplete Freund adjuvant (IFA)					
• A dose response study of HIV immunogen in IFA was conducted. Doses of 50, 100, 200, or 400 micrograms (total protein) were tested by DTH skin testing to the inactivated HIV-1 antigen. The HIV-1 immunogen was well tolerated, and the minimum dose required to induce HIV-1 DTH was 100 micrograms.					
HIV-1			HIV-1 infection	human, macaque	Wodarz2002
• Mathematical modeling is used to support the idea that T-helper cell dysfunction results in a compromised ability to maintain an anti-HIV CTL memory response. Models suggest strategies to restore CTL memory through therapy and improve long-term immunological control of the virus.					
HIV-1			HIV-1 infection, Vaccine	human	Imami2002a
Vaccine *Vector/Type:* gp120 depleted virus HZ321 (REMUNE(TM)), recombinant protein, virus-like particle, canarypox, adenovirus, DNA *Adjuvant:* CpG, IL-2, GMCSF, IL-7, IL-12, Growth Hormone, Thymosin alpha-1.					

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This review addresses the use of immunotherapy and therapeutic immunization to help chronically infected patients maintain a strong anti-HIV-1 T-cell response. The loss of anti HIV-1 proliferative responses early after infection is reviewed, as are therapeutic vaccinations, with or without HAART, and strategies for immunomodulation that can be given with or without vaccination.				
HIV-1			HIV-1 infection	human	Heeney2002
	• Review of the importance of balanced Th1 and Th2 HIV-specific CD4 T-cell responses in control of infection and for vaccination strategies.				
HIV-1			HIV-1 infection		Bernaschi2002
	• A cellular automata model was used to model the dynamics of HIV-1 infection and progression to disease. The model suggests the long aymptomatic period is due to immune escape mutants with lower viral fitness, and with AIDS resulting from a drastic reduction of the T-helper cell reservoire.				
HIV-1			Vaccine		Altes2002
	• This study employs a mathematical model to study the consequences of increasing the T-helper response through a vaccine, which would have counter-balancing effects in a new infection: a more intense response provides more help but also more target cells. The model indicates that if the infecting virus had a low replication rate, then CTLp and CD4 helper cells could control an infection. Only a vaccine that could increase CTL responsiveness could reduce viral set point with observed replication rates. • A CD4+ T-cell response without maintained CTL response was deleterious in this model.				
HIV-1			HIV-1 infection		Bajaria2002
	• This paper presents a dynamical model of HIV infection and progression that includes CD4 T-cell naive and memory populations distributed between the peripheral blood and the lymph nodes, as well as the effects of HAART. Increasing viral replication and infectivity and decreasing T-cell immunity had impact on the rate of disease progression in this model.				
HIV-1	(HZ321)		Vaccine	murine	Ayash-Rashkovsky2002
	Vaccine *Vector/Type:* gp120 depleted virus HZ321 (REMUNE(TM)) *Strain:* HZ321 *Adjuvant:* CpG, incomplete Freund's adjuvant (IFA) • Parasitic helminthic infections in humans, common in parts of Africa and Asia, can shift immune responses to Th2 responses. To model this, BALB/c mice were infected with the parasite Schistosoma mansoni, and the infected mice showed a dominant Th2 immune response. Vaccination with gp120-depleted HIV-1 viral particles and incomplete Freund's adjuvant induced Th2 responses in these mice, but this could be shifted towards a Th1 profile when CpG oligodeoxynucleotide was added to the vaccine as an immunostimulatory agent.				
HIV-1	HIV-1 except gp120		HIV-1 infection	human	Ghanekar2001
	• 12 long term non-progressors (>10 years) went on HAART, while 14 elected not to go on HAART. After a year on HAART, higher frequencies and absolute numbers of HIV-specific memory CD4+ T-cells were observed in untreated patients than patients receiving HAART therapy, tested by stimulation an proliferation responses to HIV Remune antigen (gp120 depleted vaccine). • These results indicate a control of viral replication in therapy-naive patients may be mediated by their ability to respond to recall viral antigen, and that the diminished response in treated patients may contribute to viral rebound.				
HIV-1			HIV-1 infection	human	Pido-Lopez2002
	• The thymic output in HAART-treated HIV-1 infected patients with progressive disease was studied. One patient also receiving steroid treatment therapy had a weak response in a sjTREC assay indicating a dysfunctional thymus, while four patients not on steroids had clear positive sjTREC readings after HAART. Stimulation of PBMC with multiple recall antigens including gp120, p24 and Nef and mitogens, and revealed that in the patient treated with steroids there was and induction of a Th2 type response indicated by increased levels of IL-4 secretion in response to antigen.				

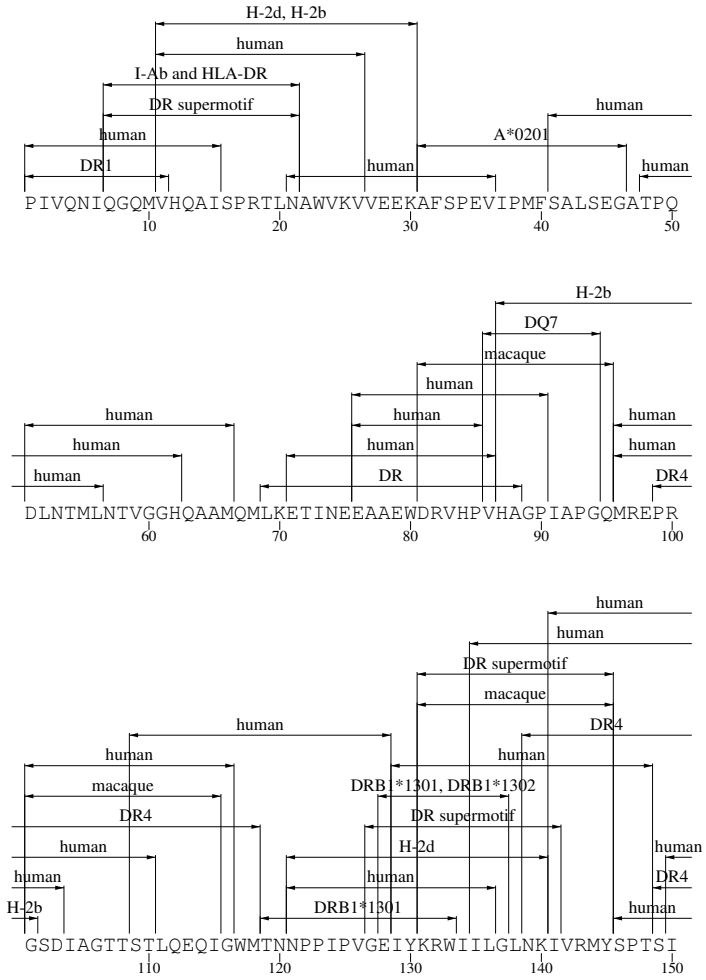
III-C Maps of T-Helper Epitope Locations Plotted by Protein

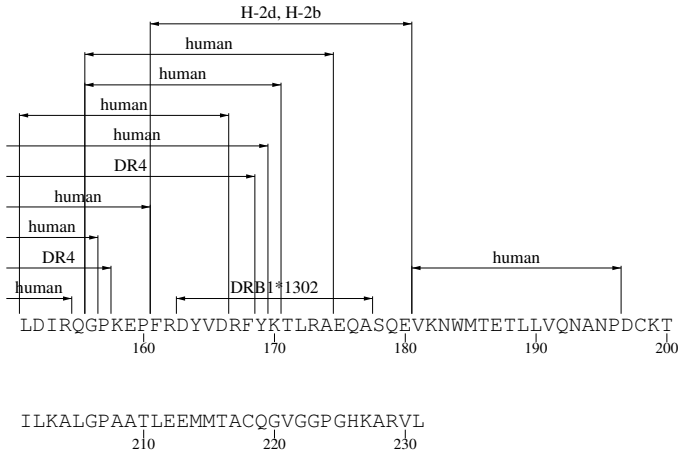
Linear helper T cell epitopes less than twenty-two amino acids long are shown.

III-C-1 p17 T-Helper Epitope Map

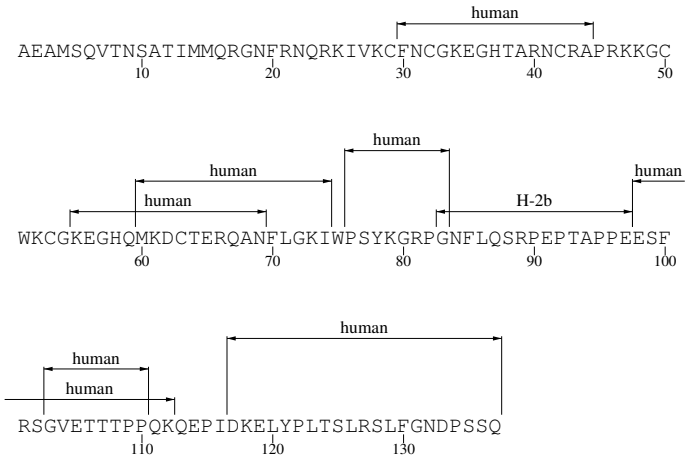


III-C-2 p24 T-Helper Epitope Map

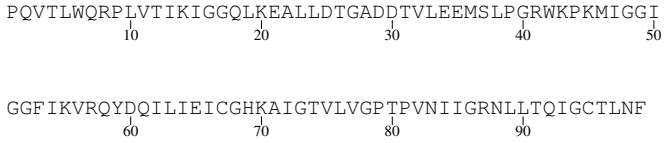




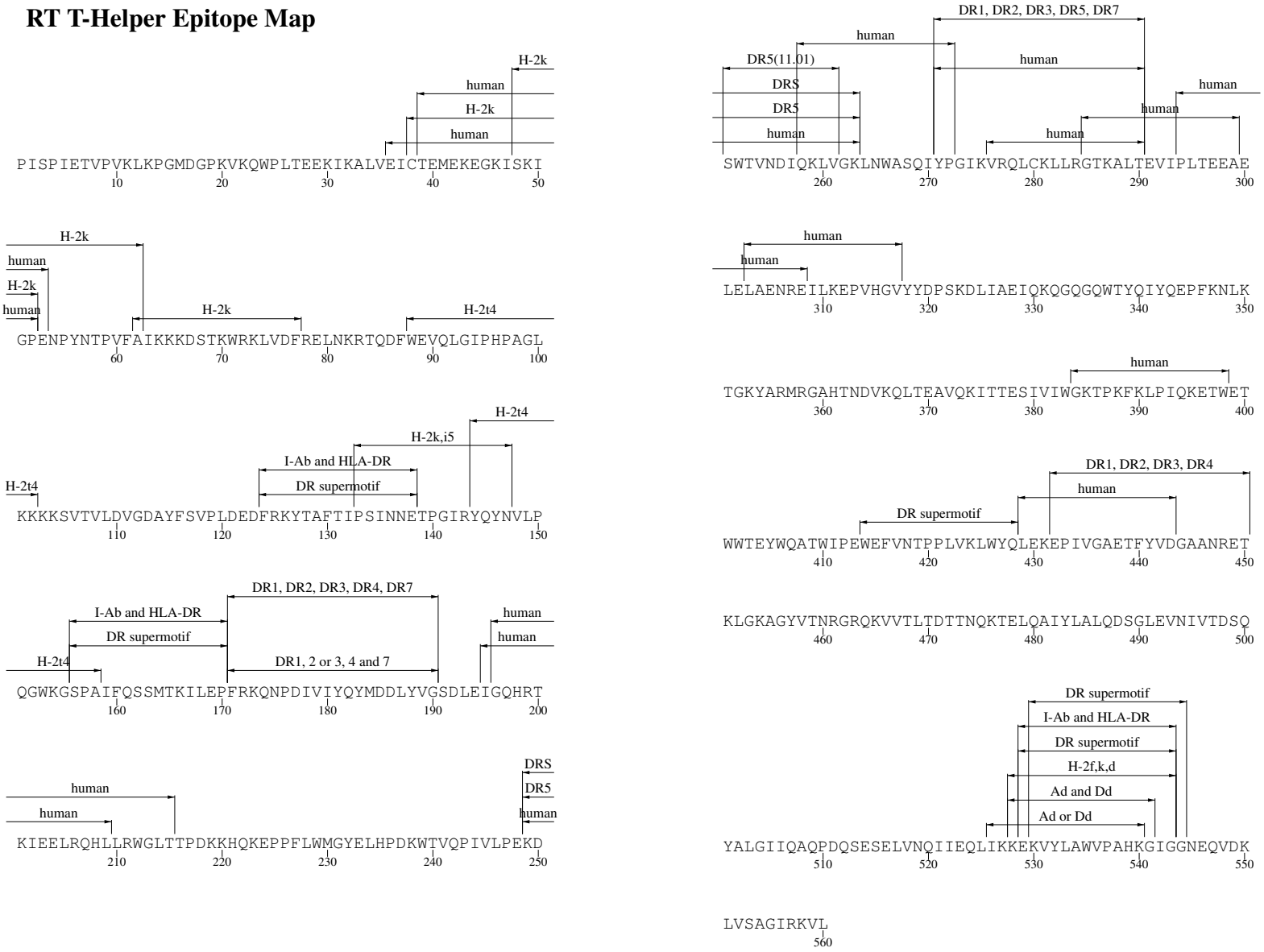
III-C-3 p2p7p1p6 T-Helper Epitope Map



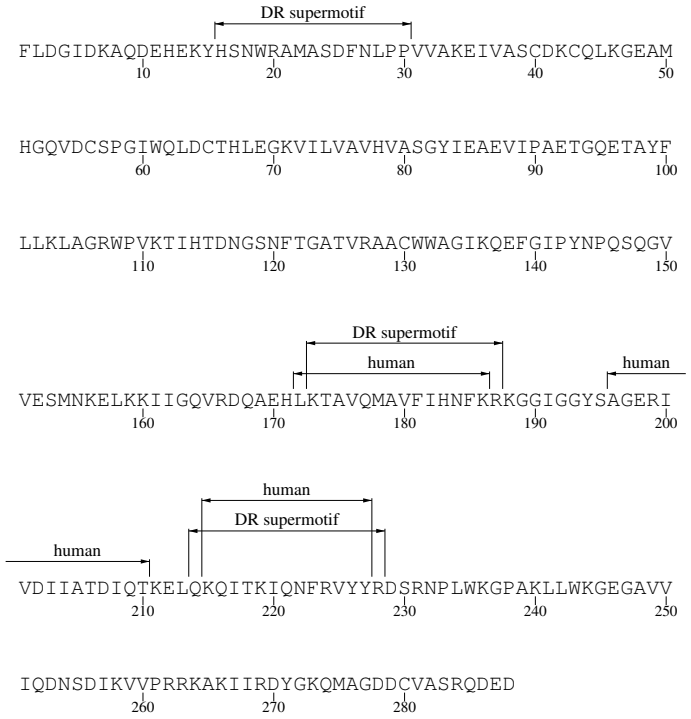
III-C-4 Protease T-Helper Epitope Map



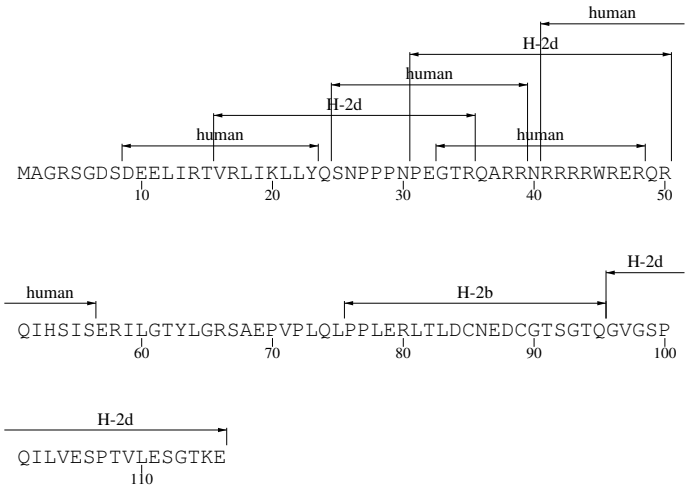
III-C-5 RT T-Helper Epitope Map



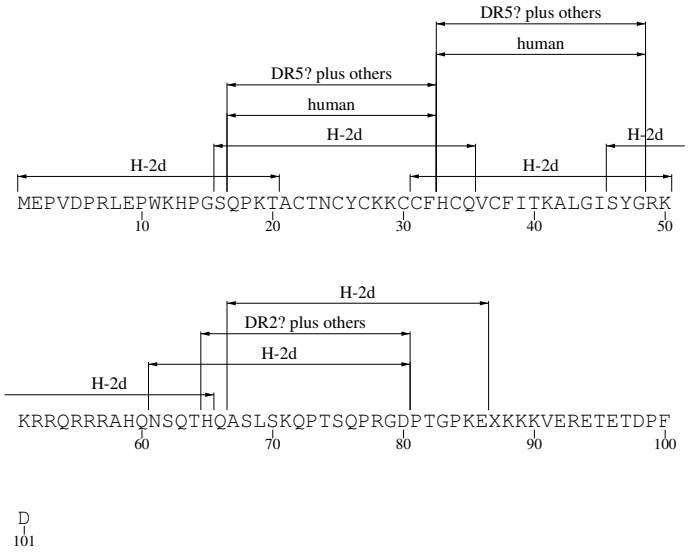
III-C-6 Integrase T-Helper Epitope Map



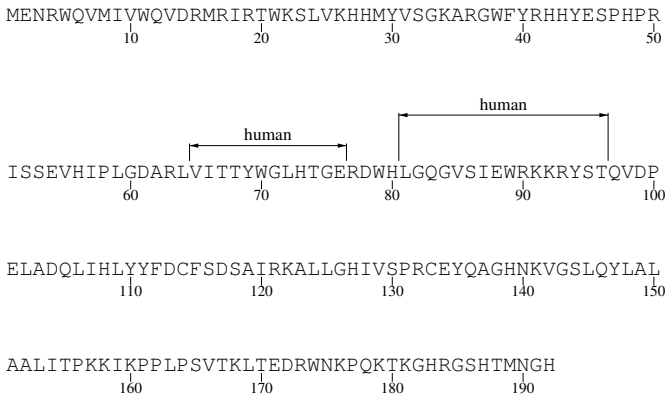
III-C-7 Rev T-Helper Epitope Map



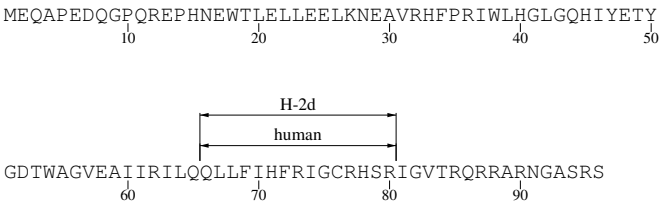
III-C-8 Tat T-Helper Epitope Map



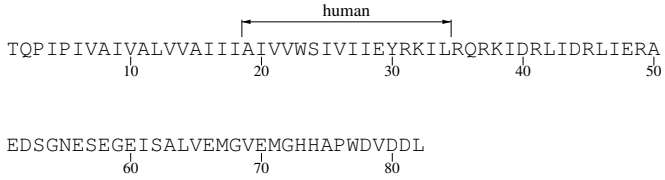
III-C-9 Vif T-Helper Epitope Map



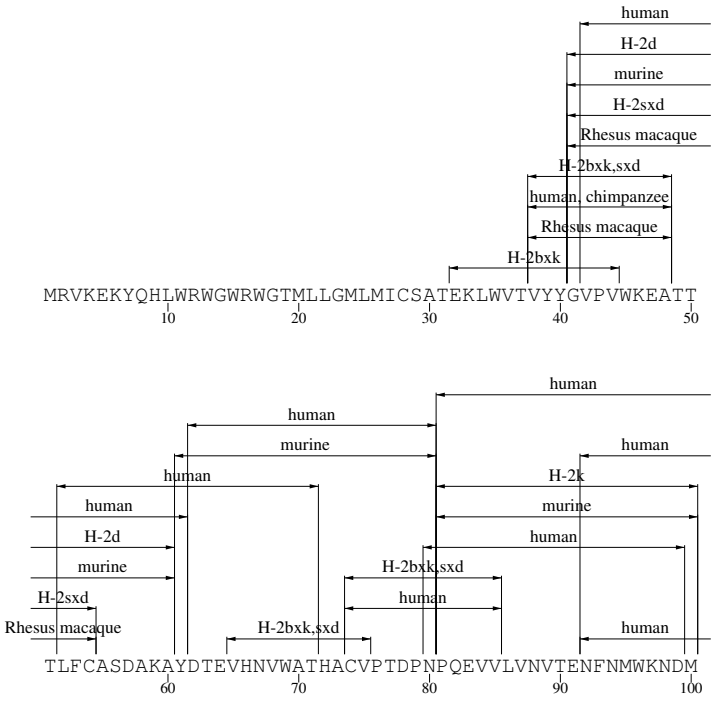
III-C-10 Vpr T-Helper Epitope Map

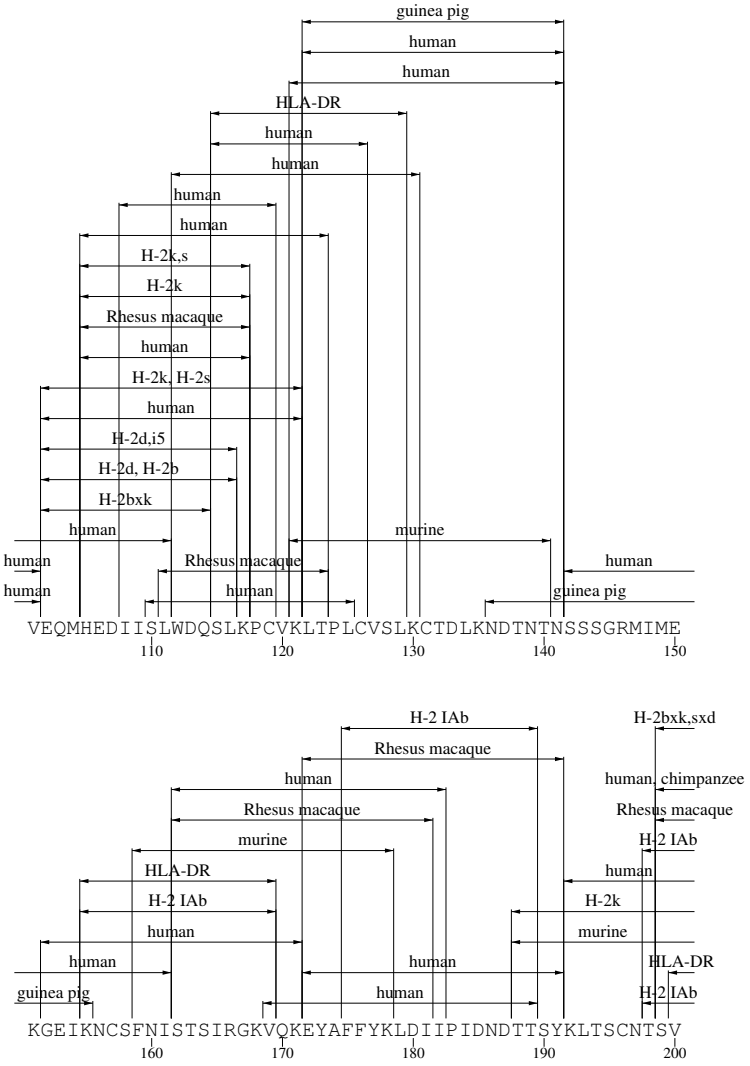


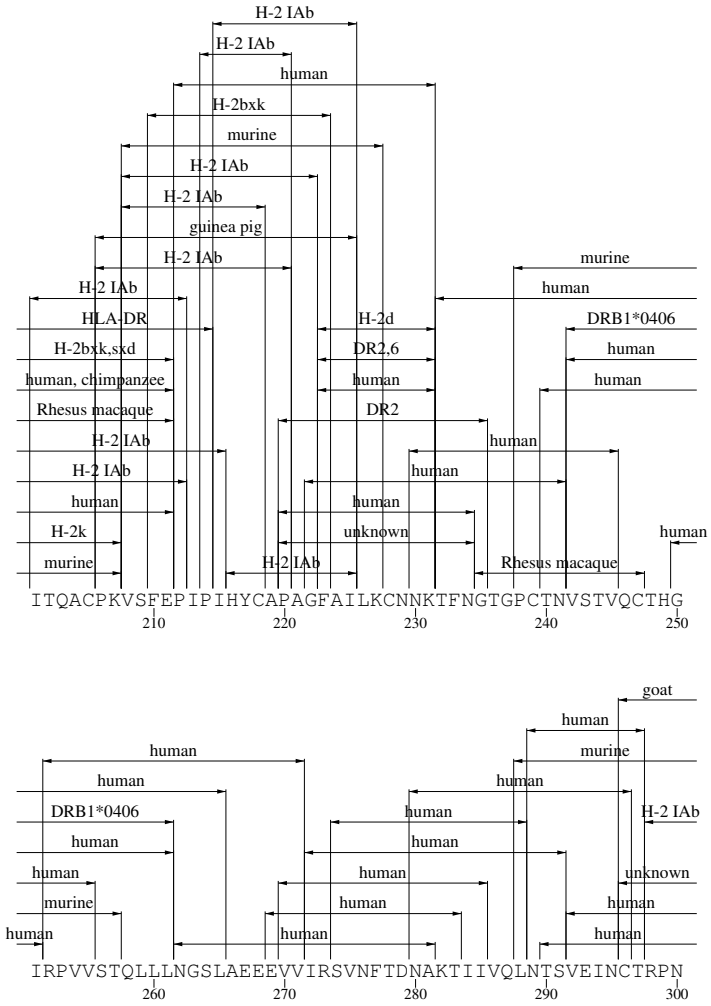
III-C-11 Vpu T-Helper Epitope Map



III-C-12 gp160 T-Helper Epitope Map



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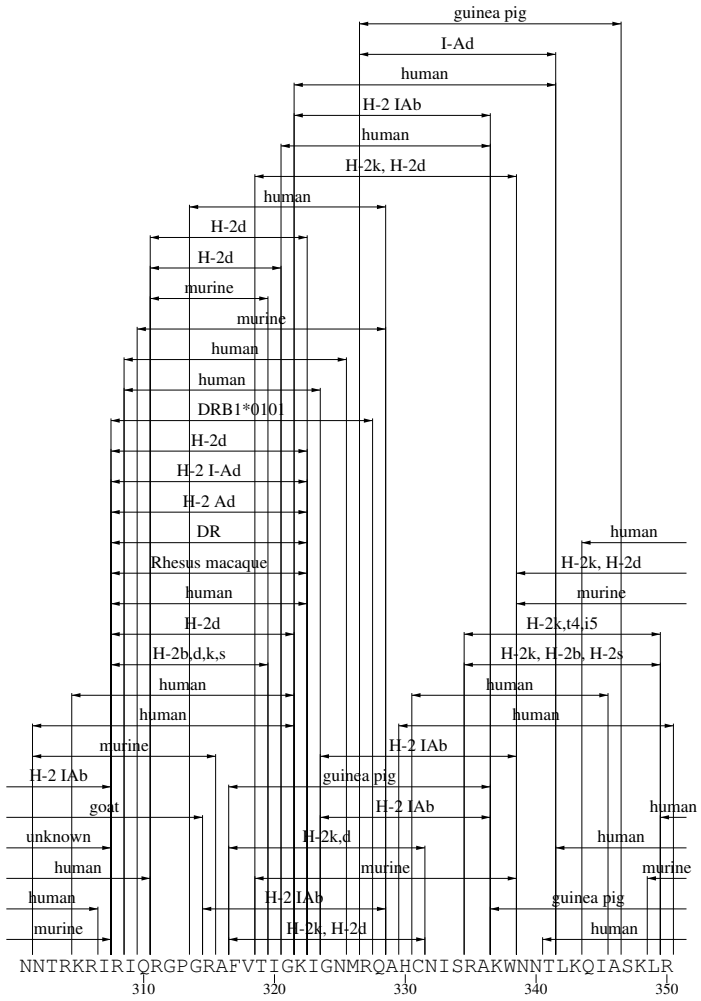
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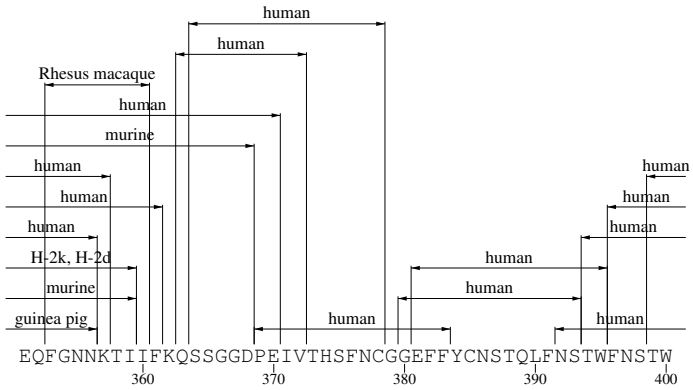
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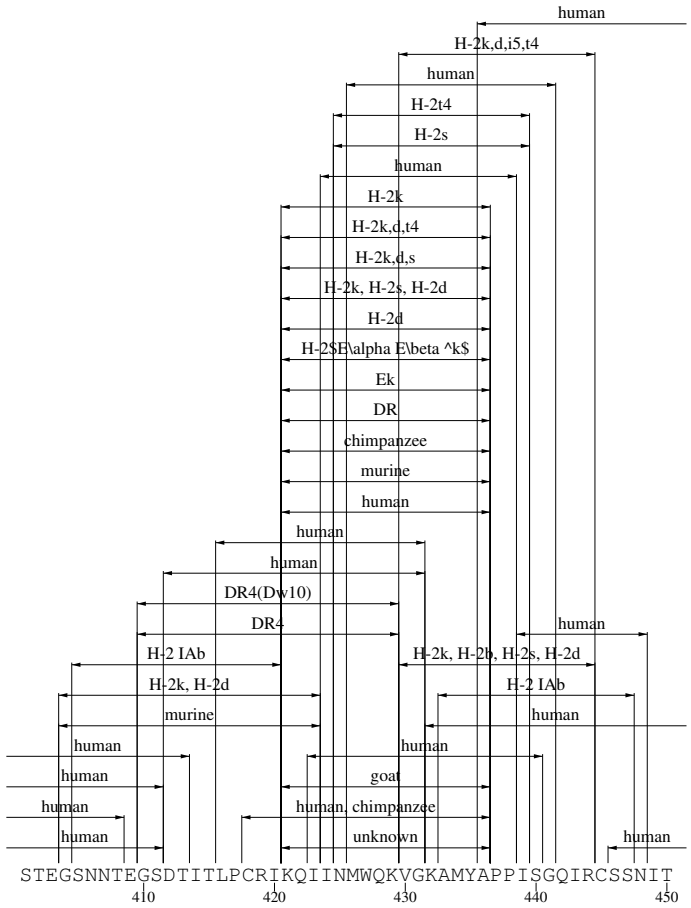
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human
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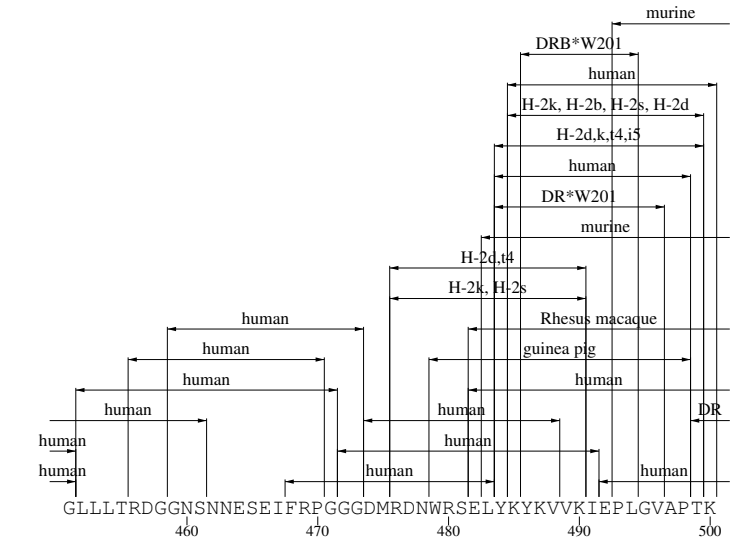
T-Helper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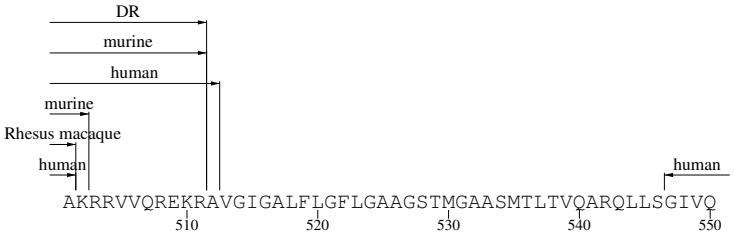
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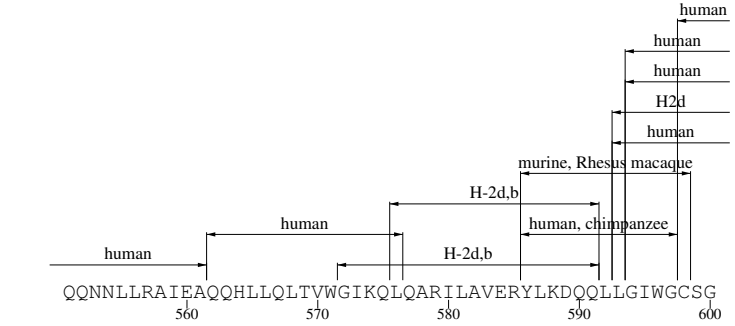
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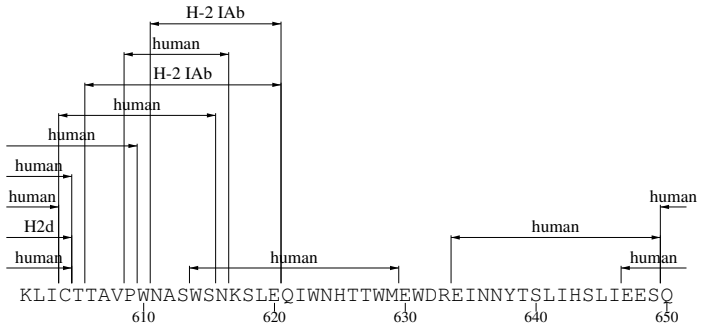
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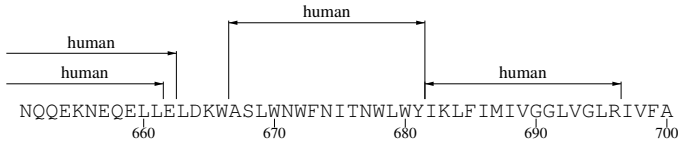
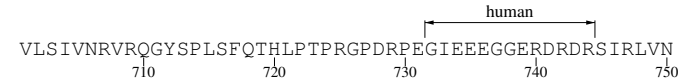
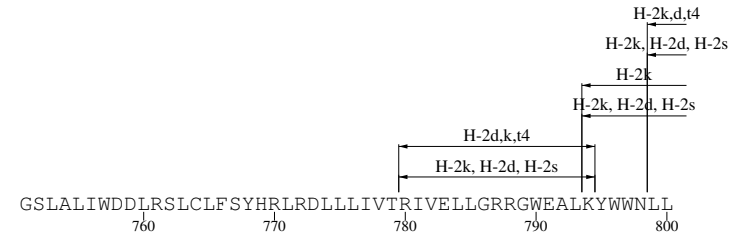
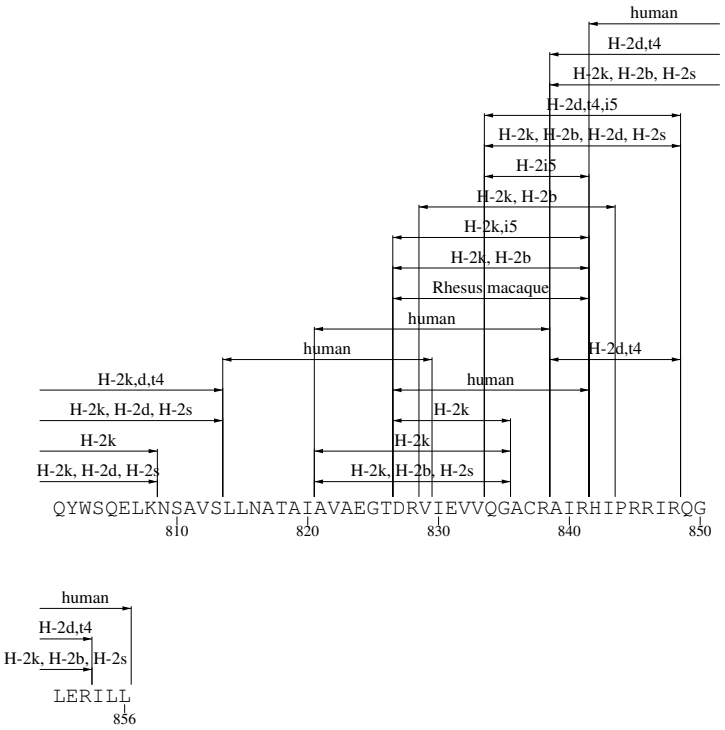
human
KLICTTAVPWNASWSNKSLEQIWNHTTWMEWDREINNYTSLIHSLIEESQ
610
620
630
640
650

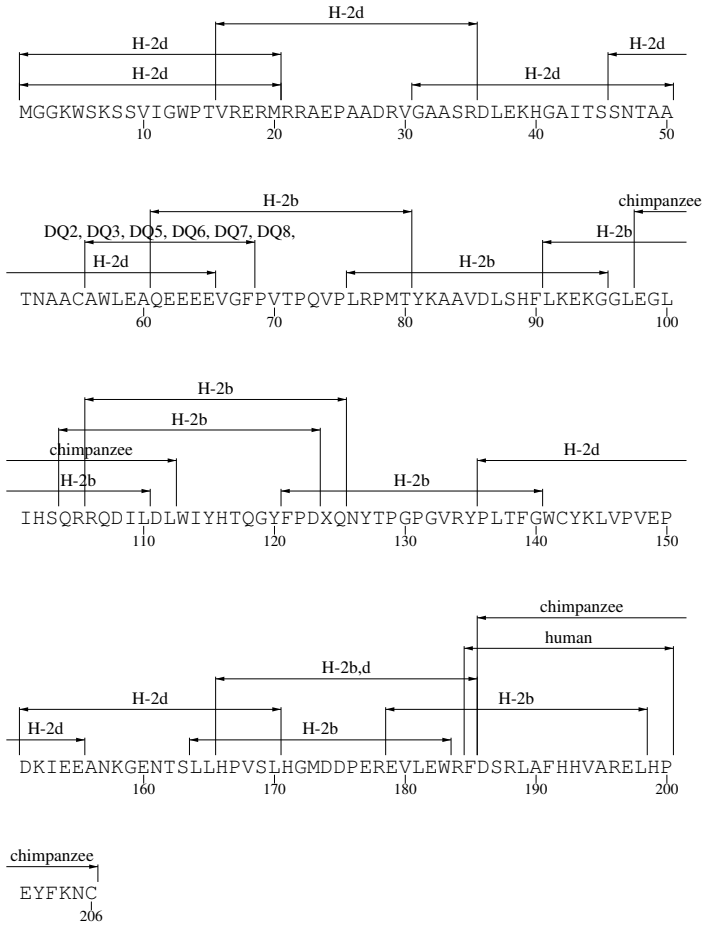

human
human
human
human
human
NQQEKNEQELLELDKWASLWNWFNITNWLWYIKLFIMIVGGLVGLRIVFA
660
670
680
690
700


human
VLSIVNRVRQGYSPLSFQTHLPTPRGPDRPEGIEEEGGERDRDRSIRLVN
710
720
730
740
750


H-2k,d,t4
H-2k, H-2d, H-2s
H-2k
H-2k, H-2d, H-2s
H-2d,k,t4
H-2k, H-2d, H-2s
GSLALIWDDLRSLCLFSYHRLRDLLLIVTRIVELLGRRGWEALKYWWNLL
760
770
780
790
800



III-C-13 Nef T-Helper Epitope Map



Part IV

HIV Antibody Binding Sites

IV-A Summary

Part IV section summarizes HIV-specific antibodies (Abs) arranged sequentially according to the location of their binding domain, organized by protein. We attempted to make this section as comprehensive as possible. For the monoclonal (MAbs) capable of binding to linear peptides, we require that the binding site be contained within a region of 30 or so amino acids to define the epitope, but not that the precise boundaries be defined. MAbs that do not bind to defined linear peptides are grouped by category at the end of each protein. Antibody categories, for example CD4 binding site (CD4BS) antibodies, are also noted in the index at the beginning of this section. Studies of polyclonal Ab responses are also included. Responses that are just characterized by binding to a protein, with no known specific binding site, are listed at the end of each protein. For more recent updates, epitope sequence alignments, and search capabilities, please see our web site: `http://hiv-web.lanl.gov/immunology`.

IV-A-1 Indices

Three indices are provided. The first provides a concise list of anti-HIV-1 MAbs by cross-competition category, with both discontinuous epitopes (for example, CD4BS) and some well known linear epitopes (for example, cluster I) summarized. The second lists the MAb's IDs in alphabetical order so one can find their location in the table. The third is a listing by order of appearance in the tables.

IV-A-2 Tables

Each MAb has an ten-part basic entry:

Number: Order of appearance in this table.

MAb ID: The name of the monoclonal antibody with synonyms in parentheses. MAbs often have several names. For example, punctuation can be lost and names are often shortened (M-70 in one paper can be M70 in another). Polyclonal responses are listed as "polyclonal" in this field.

HXB2 Location: Position of the Ab binding site relative to the viral strain HXB2 (GenBank Accession Number K03455), which is used as a reference strain throughout this publication. The numbering in this table corresponds to the protein maps. Because of HIV-1 variation the epitope may not actually be present in HXB2, rather the position in HXB2 indicates the position aligned to the epitope. HXB2 was selected as the reference strain because so many studies use HXB2, and because crystal structures for HXB2-related proteins are often available. The precise positions of an epitope on the HXB2 reference strain can be readily obtained using the interactive position locator at our web site: `http://hiv-web.lanl.gov/content/hiv-db/LOCATE_SEQ/locate.html`.

Author Location: The amino acid positions of the epitope boundaries and the reference sequence used to define the epitope are listed as given in the primary publication. Frequently, these positions as published are imprecise, and do not truly correspond to the numbering of the sequence, but they provide a reasonable guide to the peptide's approximate location in the protein. Also, in many cases, position numbers were provided but the reference sequence identification was not. Because of HIV-1's variability, position numbers require a reference strain to be meaningful. Binding sites that cannot be defined through peptide binding or interference studies are labeled as discontinuous. The approximate location on the protein, sequence number, and reference sequence are listed.

Sequence: The amino acid sequence of the binding region of interest, based on the reference strain used in the study defining the binding site. On occasions when only the position numbers and not the actual peptide sequence was specified in the original publication, we tried to fill in the peptide sequence based on the position numbers and reference strain. If the sequences were numbered inaccurately by the primary authors, or if we made a mistake in this process, we may have misrepresented the binding site's amino acid sequence. Because of this uncertainty, epitopes that were not explicitly written in the primary publication, that we determined by looking up the reference strain and the numbered location, are followed by a question mark in the table.

Neutralizing: **L**: neutralizes lab strains. **P**: neutralizes at least some primary isolates. **no**: does not neutralize. No information in this field means that neutralization was either not discussed or unresolved in the primary publications referring to the MAb.

Immunogen: The antigenic stimulus of the original B cell response. Often this is an HIV-1 infection. If a vaccine was used as the original antigenic stimulation, not a natural infection, this is noted on a separate line, and additional information about the vaccine antigen is provided as available.

Species(Isotype): The host that the antibody was generated in, and the isotype of the antibody.

References: All publications that we could find that refer to the use of a specific monoclonal antibody. First is a list of all references. Additional details for some of older references can be found in Part V, although we have tried to keep the entries self-contained since 1997. The "donor" field is meant to serve as a potential guide to a source of information about an antibody or how to obtain it, as well as to provide credit.

Notes: Describe the context of each study, and what was learned about the antibody in the study.

IV-A-3 HIV Protein Binding Site Maps

The names of MAbs and the location of well characterized linear binding sites of 21 amino acids or less are indicated relative to the protein sequences of the HXB2 clone. This map is meant to provide the relative location of epitopes on a given protein, but the HXB2 sequence may not actually bind to the MAb of interest, as it may vary relative to the sequence for which the epitope was defined. Above each linear binding site, the MAb name is given followed by the species in parentheses. Human is represented by 'h', non-human primate by 'p', mouse by 'm', and others by 'o'. More precise species designations for any given MAb can be found using the web search interface or in the tables in this section.

IV-A-4 Alignments

To conserve space, no epitope alignments are provided in this book, but they can be generated using the MAb search tool at `http://hiv-web.lanl.gov/immunology`. All epitopes are aligned to the HXB2 sequence, with the sequence used to define the epitope indicated directly above it. Sequences are sorted by their subtype and country of origin.

The master alignment files from which the epitope alignments were created are available at our web site (`http://hiv-web.lanl.gov/ALIGN_CURRENT/ALIGN-INDEX.html`). The alignments were modified in some cases to optimize the alignment relative to the defined epitope and minimize insertions and deletions; epitope alignments are generated by anchoring on the C-terminal residue. A dash indicates identity to the consensus sequence, and a period indicates an insertion made to maintain the alignment. Stop codons are indicated with a `$`, and frameshifts by a `#`, or ambiguous codons (nucleotide was `r`, `y`, or `n`) by an `x`; they are inserted to maintain the alignments. In consensus sequences an upper case letter indicates the amino acid was present in all sequences, a lower case letter indicates the amino acid was present in most sequences in a given position, and a question mark indicates two or more amino acids were represented with equal frequency.

IV-B Cross Reference Listing of MAbs

IV-B-1 MAbs by binding type

Cross reference by protein and binding type of MAb names and their order of appearance in the tables.

Binding type	MAb ID (No.)
p17	
C-term	sc-FV p17 (33)
p24	
C-term	13B5 (115)
Protease	
N-term	1696 (170)
flap region	F11.2.32 (172)
RT	
palm domain	6B9 (193)
thumb domain	5F (194), 5G (195), 7C4 (196)
Integrase	
Integrase DNA binding domain	5D9 (213), 2-19 (216), 8-22 (217), 4-20 (218), 6-19 (219)
Integrase catalytic core	7-16 (210), 4F6 (211)
N-term	1C4 (197), 2C11 (198), 2E3 (199), 3E11 (200), 3F9 (201), 5F8 (202), 6G5 (203), 7B6 (204), 7C6 (205), 6C5 (206), 4D6 (209)
Pol	
C-term	33 (244)
Vif	
C-term	TG001 (246)
Tat	
C-term	1D2F11 (252), 2D9E7 (253), 4B4C4 (254), 5G7D8 (255), NT2/4D5.24 (256), 2D9D5 (258)
N-term	NT3/2D1.1 (249), 1D9D5 (251)
Env (gp160)	
C-domain	polyclonal (601), 5B2 (669), 9G11 (670), TH-Ab1 (671), polyclonal (672), polyclonal (673), polyclonal (674), polyclonal (675)
C-term	105-306 (574), 750-D (576), 722-D (580), polyclonal (581), 1131-A (582), 858-D (583), 989-D (584), Z13 (677), 1575 (698), polyclonal (702), polyclonal (703), 1577 (705), polyclonal (706), 101-342 (853), 101-451 (854), 120-1 (855)

Binding type	MAb ID (No.)
C1	M85 (271), 7E2/4 (272), 4D4#85 (273), M92 (274), M86 (275), polyclonal (276), 133/237 (277), 133/290 (278), 133/11 (279), D/3G5 (280), D/6A11 (281), D/5E12 (282), L5.1 (283), 4A7C6 (284), 1D10 (285), B242 (286), 133/192 (287), 489.1(961) (288), 5B3 (289), B10 (290), B2 (291), C6 (292), MF49.1 (293), T1.1 (294), T7.1 (295), T9 (296), GV4D3 (297), B27 (298), B9 (299), B35 (300), D/4B5 (301), D/5A11 (302), D/6B2 (303), B18 (304), B20 (305), MF39.1 (306), 187.2.1 (307), 37.1.1(ARP 327) (308), 6D8 (309), M96 (310), MF119.1 (311), MF4.1 (312), MF53.1 (313), MF58.1 (314), MF77.1 (315), T2.1 (316), 11/65 (317), W1 (318), T11 (319), GV1A8 (320), 11 (321), 12G10 (322), 135/9 (323), 7C10 (324), C4 (325), MF46.1 (326), 212A (856), 522-149 (857), L19 (858), M90 (859), MAG 104 (860), MAG 45 (861), MAG 95 (862), MAG 97 (863), T9 (864), p7 (865)
C1-C2	L100 (866)
C1-C4	2/11c (867), A32 (868)
C1-C5	C11 (869), L81 (870)
C2	1006-30-D (367), 847-D (368), 213.1 (372), B12 (373), B13 (374), C13 (375), M89 (376), B21 (377), B23 (378), B24 (379), B25 (380), B3 (381), B26 (382), B29 (383), B36 (384), 110.E (385), 110.C (386)
C3	2H1B (340), 110.D (522), B32 (523), 2F19C (871), B2C (872), polyclonal (873)
C3, C4	ICR38.1a (533)
C4	5C2E5 (528), G3-211 (529), G3-537 (530), G3-299 (534), G3-42 (535), G3-508 (536), G3-519 (537), G3-536 (538), ICR38.8f (539), MO86/C3 (540), 13H8 (541), G45-60 (542), polyclonal (543), 1662 (544), 1663 (545), 1664 (546), 1697 (547), 1794 (548), 1804 (549), 1807 (550), 1808 (551), 1024 (874)
C5	9201 (556), 1C1 (557), 3F5 (558), 5F4/1 (559), 660-178 (560), 9301 (561), B221 (562), H11 (564), W2 (565), M38 (566), 1331A (569), 110.1 (570), 42F (571), 43F (572), RV110026 (573), GV1G2 (575), 450-D (577), 670-D (578), 23A (875), D7324 (876)
CD4BS	polyclonal (531), 1795 (532), 10/46c (877), 1027-30-D (878), 1125H (879), 120-1B1 (880), 1202-D (881), 1331E (882), 1570 (883), 1595 (884), 1599 (885), 15e (886), 205-43-1 (887), 205-46-9 (888), 21h (889), 28A11/B1 (890), 2G6 (891), 35F3/E2 (892), 38G3/A9 (893), 428 (894), 448-D (895), 44D2/D5 (896), 48-16 (897), 50-61A (898), 5145A (899), 558-D (900), 559/64-D (901), 55D5/F9 (902), 588-D (903), 654-D (904), 67G6/C4 (905), 729-D (906), 830D (907), 9CL (908), BM12 (909), D20 (910), D21 (911), D24 (912), D25 (913), D28 (914), D35 (915), D39 (916), D42 (917), D52 (918), D53 (919), D60 (920), DA48 (921), DO8i (922), F105 (923), F91 (924), GP13 (925), GP44 (926), GP68 (927), HF1.7 (928), HT5 (929), HT6 (930), HT7 (931), ICR 39.13g (932), ICR 39.3b (933), IgG1b12 (934), IgGCD4 (935), L28 (936), L33 (937), L41 (938), L42 (939), L52 (940), L72 (941), M12 (942), M13 (943), M6 (944), MAG 116 (945), MAG 12B (946), MAG 29B (947), MAG 3B (948), MAG 55 (949), MAG 72 (950), MAG 86 (951), MAG 96 (952), MTW61D (953), S1-1 (954), T13 (955), T49 (956), T56 (957), TH9 (958), anti-CD4BS summary (959), b11 (960), b13 (961), b14 (962), b3 (963), b6 (964), polyclonal (965)
CD4BS, C-term, N-term	D33 (966)
CD4BS, CD4i, V3, V2	(967)
CD4i	17b (968), 21c (969), 23e (970), 48d (971), 49e (972), X5 (973)
Env oligomer	T22 (974)
HIV-2 V3	anti-HIV-2 polyclonal (516)
Leucine zipper motif	(593), (594)

Binding type	MAb ID (No.)
N-HR, C-HR, and six-helix bundle	polyclonal (975)
N-term	polyclonal (602), 2A2 (976), AC4 (977), AD3 (978), AD3 (979), ID6 (980), ID6 (981)
V1	35D10/D2 (330), 40H2/C7 (331), 43A3/E4 (332), 43C7/B9 (333), 45D1/B7 (334), 46E3/E6 (335), 58E1/B3 (336), 64B9/A6 (337), 69D2/A1 (338), 82D3/C3 (339)
V1, V2, V3, V4, V5	polyclonal (552)
V1-V2	11/68b (982), 62c (983), CRA-6 (984), L15 (985), T52 (986), T54 (987)
V1-V2 and V3-V5	polyclonal (988)
V2	6D5 (327), B33 (328), 697-D (341), 11/4c (348), 8.22.2 (349), 12b (350), G3-136 (351), G3-4 (352), 1088 (989), 110-B (990), 1357 (991), 1361 (992), 1393A (993), 66a (994), 66c (995), 684-238 (996), 830A (997), CRA-3 (998), CRA-4 (999), L17 (1000), SC258 (1001)
V2-CD4BS	L25 (1002), L39 (1003), L40 (1004), L78 (1005)
V3	IIIB-V3-26 (387), IIIB-V3-21 (388), polyclonal (389), polyclonal (390), MO97/V3 (391), polyclonal (392), 55/1l (393), 8/38c (394), 8/64b (395), polyclonal (396), polyclonal (397), polyclonal (398), polyclonal (399), 9284 (400), polyclonal (401), polyclonal (402), polyclonal (403), polyclonal (404), MAG 109 (405), MAG 49 (406), MAG 53 (407), MAG 56 (408), 1324-E (409), polyclonal (410), MO99/V3 (411), C311E (412), 924 (414), polyclonal (415), polyclonal (416), 10F10 (417), 2C4 (418), 412-D (419), polyclonal (420), CGP 47 439 (421), polyclonal (422), 178.1 (423), 257-D (424), 311-11-D (425), 41148D (426), 391/95-D (427), Aw (428), Bw (429), DO142-10 (430), Dv (431), Fv (432), Gv (433), Hv (434), polyclonal (435), 50.1 (436), polyclonal (437), BAT123 (438), 838-D (439), 1006-15D (440), 782-D (441), 908-D (442), 1027-15D (443), F19.26-4 (444), F19.48-3 (445), F19.57-11 (446), M77 (447), SP.BAL114 (448), SP.SF2:104 (449), polyclonal (450), 19b (451), 4G10 (452), 5F7 (453), G3-523 (454), MN215 (455), Nea 9301 (456), 4117C (457), 419-D (458), 453-D (459), 504-D (460), 83.1 (461), 5023B (462), F58/D1 (463), P1/D12 (464), P4/D10 (465), IIIB-13 V3 (466), IIIB-34 V3 (467), A47/B1 (468), D59/A2 (469), G44/H7 (470), M096/V3 (471), μ5.5 (472), loop 2 (473), 268-D (474), 386-D (475), 5042A (476), 5042B (477), 418-D (478), 5021 (479), 5025B (480), 5042 (481), 110.3 (482), 110.4 (483), 110.5 (484), 58.2 (485), 537-D (487), 5020 (488), RC25 (489), 5023A (490), 110.6 (491), polyclonal (492), 10/36e (493), 10/54 (494), 11/85b (495), polyclonal (496), 0.5β (497), Cβ1, 0.5β (498), NM-01 (499), 1026 (500), 1034 (501), 59.1 (502), polyclonal (503), 10E3 (504), polyclonal (505), N11-20 (506), 5025A (507), N70-1.9b (508), 902 (509), 694/98-D (510), 9205 (514), 110.I (515), IIIB-V3-01 (517), 447-52D (681), (1006), 110.J (1007), 1334-D (1008), 2182 (1009), 2191 (1010), 2219 (1011), 2412 (1012), 2442 (1013), 2456 (1014), 39F (1015), 55/68b (1016), 5G11 (1017), 6.1 (1018), 6.7 (1019), 8.27.3 (1020), 8E11/A8 (1021), 9305 (1022), AG1121 (1023), D47 (1024), F5.5 (1025), G3-1472 (1026), K24 (1027), TH1 (1028), anti-gp120/V3 (1029), polyclonal (1030), polyclonal (1031), polyclonal (1032), polyclonal (1033), polyclonal (1034), polyclonal (1035), polyclonal (1036)
V3 discontinuous	11/75a/21/41 (1037), 41.1 (1038), 55/45a/1l (1039)
V3 mimotope	1108 (1040)
V3, V4	polyclonal (1041)
V3-C4	MO101/V3,C4 (511), polyclonal (1042)
V3-C5	MO101/V3,C4 (512), MO101/V3,C4 (513)
V3-CD4BS	D27 (1043), D56 (1044)

Binding type	MAb ID (No.)
V4	D/6D1 (518), 4D7/4 (519), 36.1(ARP 329) (520), C12 (521), polyclonal (524), B15 (525), B34 (526)
V5	polyclonal (553)
V5-C5	CRA1(ARP 323) (554), M91 (555), 8C6/1 (563)
adjacent to cluster II	2F5 (667)
alpha-helical C-HR, hairpin intermediate	98-6 (663)
carbohydrates at glycosylation residues in C2, C3, C4, and V4	2G12 (1045)
cluster I	50-69 (605), 246-D (623), 181-D (625), 240-D (627), F240 (628), D49 (629), D61 (630), T32 (631), T34 (632), 1367 (1046)
cluster II	D50 (660), 167-7 (664), ND-15G1 (665), 126-6 (1047), 1342 (1048), 1379 (1049), Fab D11 (1050), Fab D5 (1051), Fab G1 (1052), Fab M10 (1053), Fab M12 (1054), Fab M15 (1055), Fab S10 (1056), Fab S6 (1057), Fab S8 (1058), Fab S9 (1059), Fab T3 (1060), Md-1 (1061)
cluster II, six-helix bundle	167-D (666), 1281 (1062)
cluster III	Fab A9 (1063), Fab G15 (1064), Fab G5 (1065), Fab L1 (1066), Fab L11 (1067), Fab L2 (1068)
cytoplasmic domain	Chessie 8 (1069)
gp120-CD4 complex	8F101 (1070), 8F102 (1071), CG-10 (1072), CG-25 (1073), CG-4 (1074), CG-76 (1075), CG-9 (1076)
immunodominant region	3D6 (658), 105-518 (1077)
p24+gp41	31A1 (1078), 39A64 (1079), 39B86 (1080), 9303 (1081)
six helix bundle	NC-1 (1082)
Nef	
C-term	AE6 (1116), AG11 (1117), EH1 (1118), AE6 (1123)

IV-B-2 Alphabetical listing of MAbs

Cross reference of MAb names and their order of appearance in the tables. Alphanumeric sorting is symbols, digits, uppercase letters and lowercase letters.

MAb ID	No.
	593
	594
	708
	709
	710
	711
	712
	967
	1006
α(566-586)	589
μ5.5	472
0.5β	497
1-B-7	68
1-E-4	57
1-E-9	58
1.152 B3	178
1.153 G10	186
1.158 E2	179
1.160 B3	190
1.17.3	89
1.2	250
10-E-7	59
10-G-9	60
10.1	261
10/36e	493
10/46c	877
10/54	494
10/76b	344
1006-15D	440
1006-30-D	367
101-342	853
101-451	854
102-135	713
1024	874
1025	714
1026	500
1027-15D	443
1027-30-D	878
1034	501
105-134	715
105-306	574
105-518	1077
105-732	657
106/01	116
108/03	110
1088	989
10E3	504
10E7	171
10E9	716
10F10	417
11	321
11-C-5	61
11/41e	345
11/4b	346
11/4c	348
11/65	317
11/68b	982
11/75a/21/41	1037
11/85b	495
110-B	990
110.1	363
110.1	570
110.3	482
110.4	483
110.5	484
110.6	491
110.C	386
110.D	522
110.E	385
110.I	515
110.J	1007
110/015	111
1108	1040
1109/01	49
111/052	46
111/073	55
111/182	36
112/021	37
112/047	38
1125H	879
113/038	56
113/072	74
1131-A	582
115.8	633
11C10B10	105
11D11F2	106
11H9	24
12	224
12-B-4	102
120-1	855
120-16	662
120-1B1	880
1202-D	881
126-50	717
126-6	1047
1281	1062
12G-A8g2	19
12G-D7h11	20
12G-H1c7	21
12G10	322
12H-D3b3	18
12H2	718
12I-D12g2	22
12b	350
13	225
13-102-100	76
13.10	719
13/035	1086
13/042	1085
13/058	1096
1324-E	409
133/11	279
133/192	287
133/237	277
133/290	278
1331A	569
1331E	882
1334-D	1008
1342	1048
135/9	323
1357	991
1361	992
1367	1046
1379	1049
1393A	993
13B5	115
13E1	173
13H8	541
14	226
14D4E11	50
15-21	31
1570	883
1575	698
1576	685
1577	705
1578	686
1579	687
1583	688
1595	884
1599	885
15F8C7	45
15e	886
16	227
16/4/2	134
1662	544
1663	545
1664	546
167-7	664
167-D	666
1696	170
1697	547
17	208
178.1	423
1794	548
1795	532
17b	968
1804	549
1807	550
1808	551
181-D	625
183-H12-5C	135
187.2.1	307
1899	689
19	215
1907	690
1908	691
1909	692
19b	451
1A1	585
1A7	90
1B1	720
1B2C12	86
1B8.env	647
1C1	557
1C12B1	228
1C4	197
1D10	285
1D2F11	252
1D4A3	188
1D9	27
1D9D5	251
1E8	177
1F11	595
1F6	91
1F7	721
1G10	267
1G5C8	51
1G7	268
1H5	596
2-19	216
2-E-4	62
2-H-4	63
2.2B	722
2/11c	867
205-43-1	887
205-46-9	888
21	229
212A	856

213.1
2182
2191
21c
21h
2219
23A
23A5G4
23A5G5
23e
240-D
241-D
2412
2442
2456
246-D
24G3
25.3
25/03
257-D
25C2
26/028
26/76
268-D
28A11/B1
2A2
2A2/26
2A3
2A6
2C11
2C4
2D9D5
2D9E7
2E3
2E3
2E4
2F11
2F19C
2F2
2F5
2G12
2G2
2G6

372
1009
1010
969
889
1011
875
92
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970
627
136
1012
1013
1014
623
586
75
1089
424
587
1097
1090
474
890
976
604
1109
137
198
418
258
253
199
1098
1110
622
871
1106
667
1045
270
891

2H12
2H1B
3-B-7
3-H-7
30:3E5
30D
31-11
31/03
311-11-D
31710B
31A1
31D6
31G8
32
32/1.24.89
32/5.8.42
32/5.8.42
322-151
32:32K
32E7
33
33D5
35
35D10/D2
35F3/E2
36.1(ARP 329)
37.1.1(ARP 327)
38/12b
38/60b
386-D
38:9.6K
38B5/C9
38G3/A9
391/95-D
39A64
39B86
39F
39H10/A11
3A2
3A6
3B10
3D10G6
3D12

1111
340
69
25
83
723
32
1101
425
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1078
180
181
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359
112
182
244
183
231
330
892
520
308
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357
475
80
725
893
427
1079
1080
1015
726
1112
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12
94
232

3D12
3D3
3D3.B8
3D5
3D6
3D9
3E11
3E11
3E6
3F10
3F2
3F5
3F9
3G12
3G4
3H6
3H6
4
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4
4-20
406/01
40D3/C11
40H2/C7
41-1
41-1
41-2
41-3
41-6
41-7
41.1
41.4
41148D
4117C
412-D
418-D
419-D
41S-2
428
42F
43A3/E4
43C7/B9
43F
447-52D

1092
43
360
727
658
597
13
200
1108
233
1091
558
201
1095
266
262
728
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729
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1038
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426
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478
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894
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332
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681

448-D
44D2/D5
450-D
453-D
45D1/B7
46E3/E6
47-2
48-16
489.1(961)
48d
493-156
49B11/A1
49e
4A7C6
4B3
4B4C4
4C11.D8
4C9
4D4
4D4#85
4D6
4D7/4
4E10
4F6
4G10
4G2
4G9
4H2B1
4H4
5-21-3
50-61A
50-69
50.1
5020
5021
5023A
5023B
5025A
5025B
504-D
5042
5042A
5042B

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896
577
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730
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29
1083
661
898
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436
488
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476
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5145A
522-149
52G5/B9
537-D
55/1l
55/45a/1l
55/68b
558-D
559/64-D
55D5/F9
55E4/H1
56C4/C8
57B6/F1
57H5/D7
58.2
588-D
58E1/B3
59.1
5B2
5B2
5B3
5C2E5
5D9
5E2.A3k
5F
5F3
5F4/1
5F7
5F8
5G
5G11
5G7D8
6-19
6-D-12
6-E-7
6.1
6.1
6.7
60b
62c
63G4/E2
64B9/A6
654-D

899
857
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487
393
1039
1016
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138
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559
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202
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1017
255
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1018
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983
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337
904

polyclonal	813
polyclonal	814
polyclonal	815
polyclonal	816
polyclonal	817
polyclonal	818
polyclonal	819
polyclonal	820
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polyclonal	850
polyclonal	851
polyclonal	852
polyclonal	873
polyclonal	965
polyclonal	975
polyclonal	988
polyclonal	1030
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polyclonal	1042
polyclonal	1084
polyclonal	1093
polyclonal	1094
polyclonal	1099
polyclonal	1102
polyclonal	1103
polyclonal	1104
polyclonal	1114
polyclonal	1124
polyclonal	1125
polyclonal	1126
polyclonal	1127
polyclonal	1128
polyclonal	1129
polyclonal	1130
polyclonal	1131
polyclonal α577-596	591
polyclonal α598-609	646
polyclonal HIVIG	169
sc-FV p17	33

IV-B-3 MAbs by order of appearance in tables

No.	MAb ID
p17	
1	L14.17
2	polyclonal
3	32/5.8.42
4	32/5.8.42
5	HyHIV-1
6	HyHIV-2
7	HyHIV-3
8	HyHIV-4
9	HyHIV-5
10	HyHIV-6
11	32/1.24.89
12	3B10
13	3E11
14	8H10
15	HyHIV-21
16	B4f8
17	HyHIV-22
18	12H-D3b3
19	12G-A8g2
20	12G-D7h11
21	12G-H1c7
22	12I-D12g2
23	polyclonal
24	11H9
25	3-H-7
26	C5126
27	1D9
28	4C9
29	4H2B1
30	9G5
31	15-21
32	31-11
33	sc-FV p17
34	HyHIV-15
p24	
35	3A6
36	111/182
37	112/021
38	112/047
39	ID8F6
40	F5-2
41	CB-13/5
42	polyclonal
43	3D3
44	CD-4/1
45	15F8C7
46	111/052
47	polyclonal
48	91-5
49	1109/01
50	14D4E11
51	1G5C8
52	47-2
53	714/01
54	polyclonal
55	111/073
56	113/038
57	1-E-4
58	1-E-9
59	10-E-7
60	10-G-9
61	11-C-5
62	2-E-4
63	2-H-4
64	8-D-2
65	8-G-9
66	8-H-7
67	C5123
68	1-B-7
69	3-B-7
70	6-D-12
71	6-E-7
72	8-D-5
73	FF1
74	113/072
75	25.3
76	13-102-100
77	RL4.72.1
78	406/01
79	polyclonal
80	38:9.6K
81	EB1A9
82	polyclonal
83	30:3E5
84	EF7
85	LH-104-E
86	1B2C12
87	LH-104-K
88	LH-104-A
89	1.17.3
90	1A7
91	1F6
92	23A5G4
93	23A5G5
94	3D10G6
95	polyclonal
96	F5-4
97	MO9.42.2
98	MO9.50.2
99	V10
100	V107
101	LH-104-C
102	12-B-4
103	C5122
104	9A4C4
105	11C10B10
106	11D11F2
107	CD12B4
108	BE3
109	L14
110	108/03
111	110/015
112	32:32K
113	C5200
114	FH2
115	13B5
116	106/01
117	LH-104-B
118	LH-104-I
p24-p2p7p1p6	
119	LH-104-G
p2p7p1p6	
120	i5B11
121	EC6
122	M12
123	DG8
124	EB5
125	HH3
126	AD2
127	CA5
128	DF3
129	EC3
130	FC12
131	GE4
132	JB7
133	JF11
Gag	
134	16/4/2
135	183-H12-5C
136	241-D
137	2A6
138	5E2.A3k
139	71-31
140	91-6
141	98-4.3
142	98-4.9
143	AC2
144	BC1071
145	BE10
146	CD9
147	CH9B2
148	ED8
149	EH12E1
150	G11G1
151	G11H3
152	HyHIV-19
153	IE8G2
154	V7-8
155	anti-p24
156	human sera
157	polyclonal
158	polyclonal
159	polyclonal
160	polyclonal
161	polyclonal
162	polyclonal
163	polyclonal
164	polyclonal
165	polyclonal
166	polyclonal
167	polyclonal
168	polyclonal
169	polyclonal HIVIG
Protease	
170	1696
171	10E7
172	F11.2.32
173	13E1
174	8B11
175	8C10
176	8G5
RT	
177	1E8
178	1.152 B3
179	1.158 E2
180	31D6
181	31G8
182	32E7
183	33D5
184	5B2
185	polyclonal
186	1.153 G10
187	RTMAb8
188	1D4A3
189	RT6H
190	1.160 B3
191	polyclonal
192	C2003
193	6B9
194	5F
195	5G
196	7C4
Integrase	

197 1C4
198 2C11
199 2E3
200 3E11
201 3F9
202 5F8
203 6G5
204 7B6
205 7C6
206 6C5
207 8G4
208 17
209 4D6
210 7-16
211 4F6
212 anti-K159
213 5D9
214 8-6
215 19
216 2-19
217 8-22
218 4-20
219 6-19
220 7C3
221 7F11
222 8E5
223 MAb 35

Pol

224 12
225 13
226 14
227 16
228 1C12B1
229 21
230 32
231 35
232 3D12
233 3F10
234 4
235 6B9
236 7C4
237 RT-4
238 RT7O
239 RT7U
240 anti-HIV-1 RT
241 polyclonal
242 polyclonal
243 polyclonal
244 33

Vif

245 TG002
246 TG001
247 J4
248 polyclonal

Tat

249 NT3/2D1.1
250 1.2
251 1D9D5
252 1D2F11
253 2D9E7
254 4B4C4
255 5G7D8
256 NT2/4D5.24
257 L-anti-Tat
258 2D9D5

Rev

259 4G9
260 Ab2
261 10.1
262 3H6
263 8E7
264 9G2
265 Ab4
266 3G4
267 1G10
268 1G7
269 Ab3
270 2G2

gp160

271 M85
272 7E2/4
273 4D4#85
274 M92
275 M86
276 polyclonal
277 133/237
278 133/290
279 133/11
280 D/3G5
281 D/6A11
282 D/5E12
283 L5.1
284 4A7C6
285 1D10
286 B242
287 133/192
288 489.1(961)
289 5B3
290 B10
291 B2
292 C6
293 MF49.1
294 T1.1
295 T7.1
296 T9
297 GV4D3
298 B27
299 B9
300 B35
301 D/4B5
302 D/5A11
303 D/6B2
304 B18
305 B20
306 MF39.1
307 187.2.1
308 37.1.1(ARP 327)
309 6D8
310 M96
311 MF119.1
312 MF4.1
313 MF53.1
314 MF58.1
315 MF77.1
316 T2.1
317 11/65
318 W1
319 T11
320 GV1A8
321 11
322 12G10
323 135/9
324 7C10
325 C4
326 MF46.1
327 6D5
328 B33
329 polyclonal
330 35D10/D2
331 40H2/C7
332 43A3/E4
333 43C7/B9
334 45D1/B7
335 46E3/E6
336 58E1/B3
337 64B9/A6
338 69D2/A1
339 82D3/C3
340 2H1B
341 697-D
342 6C4/S
343 C108G
344 10/76b
345 11/41e
346 11/4b
347 RSD-33
348 11/4c
349 8.22.2
350 12b
351 G3-136
352 G3-4
353 BAT085
354 60b
355 74
356 38/12b
357 38/60b
358 polyclonal
359 322-151
360 3D3.B8
361 4C11.D8
362 493-156
363 110.1
364 GV4H3
365 J1
366 J3
367 1006-30-D
368 847-D
369 MF169.1
370 MF170.1
371 MF87.1
372 213.1
373 B12
374 B13
375 C13
376 M89
377 B21
378 B23
379 B24
380 B25
381 B3
382 B26
383 B29
384 B36
385 110.E
386 110.C
387 IIIB-V3-26
388 IIIB-V3-21
389 polyclonal
390 polyclonal
391 MO97/V3
392 polyclonal
393 55/1l
394 8/38c
395 8/64b
396 polyclonal
397 polyclonal
398 polyclonal
399 polyclonal
400 9284
401 polyclonal
402 polyclonal
403 polyclonal
404 polyclonal
405 MAG 109
406 MAG 49

407 MAG 53
408 MAG 56
409 1324-E
410 polyclonal
411 MO99/V3
412 C311E
413 907
414 924
415 polyclonal
416 polyclonal
417 10F10
418 2C4
419 412-D
420 polyclonal
421 CGP 47 439
422 polyclonal
423 178.1
424 257-D
425 311-11-D
426 41148D
427 391/95-D
428 Aw
429 Bw
430 DO142-10
431 Dv
432 Fv
433 Gv
434 Hv
435 polyclonal
436 50.1
437 polyclonal
438 BAT123
439 838-D
440 1006-15D
441 782-D
442 908-D
443 1027-15D
444 F19.26-4
445 F19.48-3
446 F19.57-11
447 M77
448 SP.BAL114
449 SP.SF2:104
450 polyclonal
451 19b
452 4G10
453 5F7
454 G3-523
455 MN215
456 Nea 9301
457 4117C
458 419-D
459 453-D
460 504-D
461 83.1
462 5023B
463 F58/D1
464 P1/D12
465 P4/D10
466 IIIB-13 V3
467 IIIB-34 V3
468 A47/B1
469 D59/A2
470 G44/H7
471 M096/V3
472 μ5.5
473 loop 2
474 268-D
475 386-D
476 5042A
477 5042B
478 418-D
479 5021
480 5025B
481 5042
482 110.3
483 110.4
484 110.5
485 58.2
486 polyclonal
487 537-D
488 5020
489 RC25
490 5023A
491 110.6
492 polyclonal
493 10/36e
494 10/54
495 11/85b
496 polyclonal
497 0.5β
498 Cβ1, 0.5β
499 NM-01
500 1026
501 1034
502 59.1
503 polyclonal
504 10E3
505 polyclonal
506 N11-20
507 5025A
508 N70-1.9b
509 902
510 694/98-D
511 MO101/V3,C4
512 MO101/V3,C4
513 MO101/V3,C4
514 9205
515 110.I
516 anti-HIV-2 polyclonal
517 IIIB-V3-01
518 D/6D1
519 4D7/4
520 36.1(ARP 329)
521 C12
522 110.D
523 B32
524 polyclonal
525 B15
526 B34
527 7F11
528 5C2E5
529 G3-211
530 G3-537
531 polyclonal
532 1795
533 ICR38.1a
534 G3-299
535 G3-42
536 G3-508
537 G3-519
538 G3-536
539 ICR38.8f
540 MO86/C3
541 13H8
542 G45-60
543 polyclonal
544 1662
545 1663
546 1664
547 1697
548 1794
549 1804
550 1807
551 1808
552 polyclonal
553 polyclonal
554 CRA1(ARP 323)
555 M91
556 9201
557 1C1
558 3F5
559 5F4/1
560 660-178
561 9301
562 B221
563 8C6/1
564 H11
565 W2
566 M38
567 Chim 1
568 polyclonal
569 1331A
570 110.1
571 42F
572 43F
573 RV110026
574 105-306
575 GV1G2
576 750-D
577 450-D
578 670-D
579 polyclonal
580 722-D
581 polyclonal
582 1131-A
583 858-D
584 989-D
585 1A1
586 24G3
587 25C2
588 5F3
589 α(566-586)
590 PC5009
591 polyclonal α577-596
592 polyclonal
593
594
595 1F11
596 1H5
597 3D9
598 4B3
599 4D4
600 4G2
601 polyclonal
602 polyclonal
603 polyclonal
604 2A2/26
605 50-69
606 9-11
607 98-43
608 41-1
609 41.4
610 Fab A1
611 Fab A4
612 Fab M12B
613 Fab M26B
614 Fab M8B
615 Fab T2
616 86
617 polyclonal
618 V10-9
619 polyclonal
620 polyclonal
621 polyclonal

622 2F11
623 246-D
624 9G5A
625 181-D
626 polyclonal
627 240-D
628 F240
629 D49
630 D61
631 T32
632 T34
633 115.8
634 M-1
635 M-11
636 M-13
637 M-2
638 M-22
639 M-24
640 M-25
641 M-28
642 M-29
643 M-36
644 M-4
645 M-6
646 polyclonal α598-609
647 1B8.env
648 polyclonal
649 clone 3
650 4
651 41-6
652 41-7
653 68.1
654 68.11
655 75
656 polyclonal
657 105-732
658 3D6
659 F172-D8
660 D50
661 5-21-3
662 120-16
663 98-6
664 167-7
665 ND-15G1
666 167-D
667 2F5
668 polyclonal
669 5B2
670 9G11
671 TH-Ab1
672 polyclonal
673 polyclonal
674 polyclonal
675 polyclonal
676 4E10
677 Z13
678 B30
679 polyclonal
680 41S-2
681 447-52D
682 C8
683 B31
684 B33
685 1576
686 1578
687 1579
688 1583
689 1899
690 1907
691 1908
692 1909
693 41-1
694 41-2
695 41-3
696 ED6
697 LA9 (121-134)
698 1575
699 88-158/02
700 88-158/022
701 88-158/079
702 polyclonal
703 polyclonal
704 B8
705 1577
706 polyclonal
707 DZ

Env

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713 102-135
714 1025
715 105-134
716 10E9
717 126-50
718 12H2
719 13.10
720 1B1
721 1F7
722 2.2B
723 30D
724 31710B
725 38B5/C9
726 39H10/A11
727 3D5
728 3H6
729 40D3/C11
730 49B11/A1
731 52G5/B9
732 55E4/H1
733 56C4/C8
734 57B6/F1
735 57H5/D7
736 63G4/E2
737 65B12/C5
738 6E10
739 7-1054
740 7B2
741 85G11/D8
742 87E4/A8
743 97B1/E8
744 A9
745 B4
746 B5
747 B6
748 BAT267
749 BAT401
750 BAT509
751 C31
752 D1
753 D12
754 D16
755 D4
756 D43
757 F223
758 F285
759 F7
760 Fab A12
761 Fab A2
762 Fab L9
763 G12
764 G2
765 H2
766 H8
767 HBW4
768 HIVIG
769 IVI-4G6
770 K14
771 M25
772 MAG 6B
773 MO28
774 MO30
775 MO43
776 N2-4
777 N70-2.3a
778 P43110
779 P5-3
780 T15G1
781 T20
782 T27
783 T3
784 T30
785 T4
786 multiple Fabs
787 multiple MAbs
788 multiple MAbs
789 multiple MAbs
790 polyclonal
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848 polyclonal
849 polyclonal
850 polyclonal
851 polyclonal
852 polyclonal
853 101-342
854 101-451
855 120-1
856 212A
857 522-149
858 L19
859 M90
860 MAG 104
861 MAG 45
862 MAG 95
863 MAG 97
864 T9
865 p7
866 L100
867 2/11c
868 A32
869 C11
870 L81
871 2F19C
872 B2C
873 polyclonal
874 1024
875 23A
876 D7324
877 10/46c
878 1027-30-D
879 1125H
880 120-1B1
881 1202-D
882 1331E
883 1570
884 1595
885 1599
886 15e
887 205-43-1
888 205-46-9
889 21h
890 28A11/B1
891 2G6
892 35F3/E2
893 38G3/A9
894 428
895 448-D
896 44D2/D5
897 48-16
898 50-61A
899 5145A
900 558-D
901 559/64-D
902 55D5/F9
903 588-D
904 654-D
905 67G6/C4
906 729-D
907 830D
908 9CL
909 BM12
910 D20
911 D21
912 D24
913 D25
914 D28
915 D35
916 D39
917 D42
918 D52
919 D53
920 D60
921 DA48
922 DO8i
923 F105
924 F91
925 GP13
926 GP44
927 GP68
928 HF1.7
929 HT5
930 HT6
931 HT7
932 ICR 39.13g
933 ICR 39.3b
934 IgG1b12
935 IgGCD4
936 L28
937 L33
938 L41
939 L42
940 L52
941 L72
942 M12
943 M13
944 M6
945 MAG 116
946 MAG 12B
947 MAG 29B
948 MAG 3B
949 MAG 55
950 MAG 72
951 MAG 86
952 MAG 96
953 MTW61D
954 S1-1
955 T13
956 T49
957 T56
958 TH9
959 anti-CD4BS summary
960 b11
961 b13
962 b14
963 b3
964 b6
965 polyclonal
966 D33
967
968 17b
969 21c
970 23e
971 48d
972 49e
973 X5
974 T22
975 polyclonal
976 2A2
977 AC4
978 AD3
979 AD3
980 ID6
981 ID6
982 11/68b
983 62c
984 CRA-6
985 L15
986 T52
987 T54
988 polyclonal
989 1088
990 110-B
991 1357
992 1361
993 1393A
994 66a
995 66c
996 684-238
997 830A
998 CRA-3
999 CRA-4
1000 L17
1001 SC258
1002 L25
1003 L39
1004 L40
1005 L78
1006
1007 110.J
1008 1334-D
1009 2182
1010 2191
1011 2219
1012 2412
1013 2442
1014 2456
1015 39F
1016 55/68b
1017 5G11
1018 6.1
1019 6.7
1020 8.27.3
1021 8E11/A8
1022 9305
1023 AG1121
1024 D47
1025 F5.5
1026 G3-1472
1027 K24
1028 TH1
1029 anti-gp120/V3
1030 polyclonal
1031 polyclonal
1032 polyclonal
1033 polyclonal
1034 polyclonal
1035 polyclonal
1036 polyclonal
1037 11/75a/21/41
1038 41.1
1039 55/45a/1l
1040 1108
1041 polyclonal
1042 polyclonal
1043 D27
1044 D56
1045 2G12
1046 1367
1047 126-6
1048 1342
1049 1379
1050 Fab D11

1051 Fab D5
1052 Fab G1
1053 Fab M10
1054 Fab M12
1055 Fab M15
1056 Fab S10
1057 Fab S6
1058 Fab S8
1059 Fab S9
1060 Fab T3
1061 Md-1
1062 1281
1063 Fab A9
1064 Fab G15
1065 Fab G5
1066 Fab L1
1067 Fab L11
1068 Fab L2
1069 Chessie 8
1070 8F101
1071 8F102
1072 CG-10
1073 CG-25
1074 CG-4
1075 CG-76
1076 CG-9
1077 105-518
1078 31A1
1079 39A64
1080 39B86
1081 9303
1082 NC-1

Nef

1083 4H4
1084 polyclonal
1085 13/042
1086 13/035
1087 AM5C6
1088 AM5C6
1089 25/03
1090 26/76
1091 3F2
1092 3D12
1093 polyclonal
1094 polyclonal
1095 3G12
1096 13/058
1097 26/028
1098 2E3
1099 polyclonal
1100 F14.11
1101 31/03
1102 polyclonal
1103 polyclonal
1104 polyclonal
1105 F1
1106 2F2
1107 E9
1108 3E6
1109 2A3
1110 2E4
1111 2H12
1112 3A2
1113 NF1A1
1114 polyclonal
1115 E7
1116 AE6
1117 AG11
1118 EH1
1119 6.1
1120 NF2B2
1121 NF3A3
1122 NF8B4
1123 AE6

HIV-1

1124 polyclonal
1125 polyclonal
1126 polyclonal
1127 polyclonal
1128 polyclonal
1129 polyclonal
1130 polyclonal
1131 polyclonal

IV-C HIV Antibodies Tables

All HIV MAbs and polyclonal Abs that bind to linear epitopes 30 amino acids or less in length arranged by protein position. The table entries are sorted in a nested way—first by protein, then by HXB2 start location, then by antibody type and finally by antibody name. Abs that bind to conformational epitopes or with unknown epitopes are listed at the end of each protein section.

IV-C-1 p17 Antibodies

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
1	L14.17	p17 (11–25)	p17 (11–25 BRU)	GELDRWEKIRLRPGG	no	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* viral lysate *Strain:* BRU *HIV component:* virus **References** Tatsumi1990, Robert-Hebmann1992b, Robert-Hebmann1992a					
2	polyclonal	p17 (11–25)	p17 (11–25 LAI)	GELDRWEKIRLRPGG	N	Vaccine	mouse
		Vaccine *Vector/Type:* recombinant protein, virus-like particle *Strain:* LAI *HIV component:* p24, p17, p55 *Adjuvant:* Freund's adjuvant **References** Truong1997 • An ELISA assay was used to study a panel of Gag peptides – mature p24 CA epitopes mapped to residues 176-192, 201-218, 233-253, 285-304, and were recognized by antibodies elicited by rp24CA – one p17MA epitope, residues 11-25, and one p24CA epitope, residues 176-192, were recognized by antibodies raised against anti-p55 virus-like particles, suggesting a differentantigenic properties for p24CA and p17MA antibodies depending on whether they are produced against the mature soluble protein or the immature assembled form of the gag proteins [Truong1997]					
3	32/5.8.42	p17 (12–19 + 100–105)	p17 (12–19 IIIB)	ELDRWEKI+ALDKIE	no	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* viral lysate **References** Papsidero1989 • 32/5.8.42: Binds to two discontinuous regions, positions 12-19 and 100-105, peptides ELDRWEKI and ALDKIE – inhibited infectivity of cell free virus [Papsidero1989]					
4	32/5.8.42	p17 (12–19 + 100–105)	p17 (IIIB)	ELDRWEKI+ALDKIE	no	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* viral lysate *HIV component:* virus **References** Papsidero1989 • 32/5.8.42: Inhibited infectivity of cell free virus – bound to two peptides, ELDRWEKI and ALDKIE, at positions 12-19 + 100-105 [Papsidero1989]					
5	HyHIV-1	p17 (12–29)	p17 (12–29 JMH1)	ELDKWEKIRLRPGGKTLY	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* p17 **References** Liu1995, Ota1998b • HyHIV-1: This paper compares the results of affinity constant (Ka) measurements of anti-p17 MAbs using double Ab methods versus the faster, isotope-free BIAcore system, and results were found to be similar for HyHIV-(1-6) – six MAbs all bind to the first alpha helix of p17, a functional domain for both membrane binding and nuclear localization [Ota1998b]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
6	HyHIV-2	p17 (12–29)	p17 (12–29 JMH1)	ELDKWEKIRLRPGGKTLY	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* p17					
		References Liu1995, Ota1998b					
		• HyHIV-2: This paper compares the results of affinity constant (Ka) measurements of anti-p17 MAbs using double Ab methods versus the faster, isotope-free BIAcore system, and results were found to be similar for HyHIV-(1-6) – six MAbs all bind to the first alpha helix of p17, a functional domain for both membrane binding and nuclear localization [Ota1998b]					
7	HyHIV-3	p17 (12–29)	p17 (12–29 JMH1)	ELDKWEKIRLRPGGKTLY	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* p17					
		References Liu1995, Ota1998b					
		• HyHIV-3: This paper compares the results of affinity constant (Ka) measurements of anti-p17 MAbs using double Ab methods versus the faster, isotope-free BIAcore system, and results were found to be similar for HyHIV-(1-6) – six MAbs all bind to the first alpha helix of p17, a functional domain for both membrane binding and nuclear localization [Ota1998b]					
8	HyHIV-4	p17 (12–29)	p17 (12–29 JMH1)	ELDKWEKIRLRPGGKTLY?	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* p17					
		References Liu1995, Ota1998a, Ota1998b					
		• HyHIV-4: epitope uncertain, based on the best estimate from JMH1 sequence– Ka is 1.8 x 107 M-1 for rec p17 – stains the surface of infected cells indicating the antigen is exposed at the cell surface [Ota1998a]					
		• HyHIV-4: This paper compares the results of affinity constant (Ka) measurements of anti-p17 MAbs using double Ab methods versus the faster, isotope-free BIAcore system, and results were found to be similar for HyHIV-(1-6) – six MAbs all bind to the first alpha helix of p17, a functional domain for both membrane binding and nuclear localization [Ota1998b]					
9	HyHIV-5	p17 (12–29)	p17 (12–29 JMH1)	ELDKWEKIRLRPGGKTLY	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* p17					
		References Liu1995, Ota1998b					
		• HyHIV-5: This paper compares the results of affinity constant (Ka) measurements of anti-p17 MAbs using double Ab methods versus the faster, isotope-free BIAcore system, and results were found to be similar for HyHIV-(1-6) – six MAbs all bind to the first alpha helix of p17, a functional domain for both membrane binding and nuclear localization [Ota1998b]					
10	HyHIV-6	p17 (12–29)	p17 (12–29 JMH1)	ELDKWEKIRLRPGGKTLY	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* p17					
		References Liu1995, Ota1998b					
		• HyHIV-6: This paper compares the results of affinity constant (Ka) measurements of anti-p17 MAbs using double Ab methods versus the faster, isotope-free BIAcore system, and results were found to be similar for HyHIV-(1-6) – six MAbs all bind to the first alpha helix of p17, a functional domain for both membrane binding and nuclear localization [Ota1998b]					
11	32/1.24.89	p17 (17–22)	p17 (17–22 IIIB)	EKIRLR	L	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* viral lysate					
		References Papsidero1989					
		• 32/1.24.89: Inhibited infectivity of cell free virus [Papsidero1989]					
12	3B10	p17 (19–38)	p17 (19–38 SIVmac)	IRLPGGKKKYMLKHVVWAA	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* inactivated virus *Strain:* AGM TYO-7 *HIV component:* virus					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Otteken1992 • 3B10: Recognized an epitope present on HIV-2/SIVmac (MAC251/32H) , SIVagm, HIV-1, and SIVmnd, demonstrating that the matrix protein of all nine HIV and SIV isolates tested in this study expresses at least one conserved immunogenic epitope recognized serologically [Otteken1992]					
13	3E11	p17 (19–38)	p17 (19–38 SIVmac)	IRLPGGKKKYMLKHVVWAA	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* inactivated virus *Strain:* AGM TYO-7 *HIV component:* virus **References** Otteken1992, Nilsen1996 • 3E11: There is another MAb with this ID that recognizes integrase [Nilsen1996] • 3E11: Recognized an epitope present on HIV-2/SIVmac (MAC251/32H), SIVagm, HIV-1, and SIVmnd, demonstrating that the matrix protein of all nine HIV and SIV isolates tested in this study expresses at least one highly conserved immunogenic epitope [Otteken1992]					
14	8H10	p17 (30–52)	p17 (30–52 JMH1)	KLKHIVWASRELERFAVNPGLLE		Vaccine	murine (IgM)
		Vaccine *Vector/Type:* peptide *Strain:* JMH-1 *HIV component:* p17 *Adjuvant:* BSA **References** Ota1999a, Ota1999b • 8H10: The p17 MAb also can bind to the V3 loop [Ota1999a] • 8H10: Inhibits viral replication of the HIV-1 infected MT-4 cells by decreasing p17 DNA levels in the infected cells, and the effect of growing the 8H10 hybridoma in co-culture with HIV-1 infected MT-4 cells was studied [Ota1999b]					
15	HyHIV-21	p17 (30–52)	p17 (30–52 JMH1)	KLKHIIWASRELERFAVNPGLLE	no	Vaccine	murine (IgG2a)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* p17 **References** Liu1995, Ota1998a • HyHIV-21: epitope uncertain, based on the best estimate from JMH1 sequence – Ka is 3.6 x 106 M-1 for rec p17 – stains the surface of infected cells indicating the antigen is exposed at the cell surface –inhibited growth of HIV-1 JMH1 in MT-4 cells when added 24 hours after the initial culture [Ota1998a]					
16	B4f8	p17 (51–65)	p17 (51–65)	LETSEGCRQILGQLQ	no	Vaccine	rat (IgG2a)
		Vaccine *Vector/Type:* infected-cell lysate *Strain:* IIIB *HIV component:* virus **References** Shang1991 • -B4f8: Did not bind live infected cells, only cells that had been made permeable with acetone [Shang1991]					
17	HyHIV-22	p17 (52–83)	p17 (53–87 JMH1)	ETSEGCRQILGQRQPSLQTGSEELR-SLYNTIH	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* p17 **References** Liu1995, Ota1998a • HyHIV-22: epitope uncertain, based on the best estimate from JMH1 sequence – stains the surface of infected cells indicating the antigen is exposed at the cell surface – Ka is 2.3 x 105 M-1 for rec p17 [Ota1998a]					
18	12H-D3b3	p17 (62–78)	p17 (62–78)	GQLQPSLQTGSEELRSL	no	Vaccine	rat (IgG2a)
		Vaccine *Vector/Type:* infected-cell lysate *Strain:* IIIB *HIV component:* virus **References** Shang1991 • 12H-D3b3: Did not bind live infected cells, only cells that had been made permeable with acetone [Shang1991]					
19	12G-A8g2	p17 (86–115)	p17 (86–115)	YCVHQRIEIKDTKEALDKIEEEQNK-SKKKA	no	Vaccine	rat (IgG2a)
		Vaccine *Vector/Type:* infected-cell lysate *Strain:* IIIB *HIV component:* virus **References** Shang1991, Maksiutov2002					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 12G-A8g2: Bound to 30-mer, but not to internal peptides – did not bind live infected cells – antigenic domain known as HPG30 [Shang1991] • 12G-A8g2: This epitope is similar to a fragment of the human protein CD40 ligand TNF-related activation protein(T-cell antigen GP39) (CD154), LDKIEDERN, as well as to a fragment of Lens-epithelium-derived growth factor, DIITEEDKSKKKGQ [Maksiutov2002].					
20	12G-D7h11	p17 (86–115)	p17 (86–115)	YCVHQRIEIKDTKEALDKIEEEQNK-SKKKA	no	Vaccine	rat (IgG2a)
		Vaccine *Vector/Type:* infected-cell lysate *Strain:* IIIB *HIV component:* virus **References** Shang1991, Maksiutov2002 • 12G-D7h11: Bound to 30-mer, but not to internal peptides – did not bind live infected cells – antigenic domain known as HPG30 [Shang1991] • 12G-D7h11: This epitope is similar to a fragment of the human protein CD40 ligand TNF-related activation protein (T-cell antigen GP39) (CD154), LDKIEDERN, as well as to a fragment of Lens-epithelium-derived growth factor, DIITEEDKSKKKGQ [Maksiutov2002].					
21	12G-H1c7	p17 (86–115)	p17 (86–115)	YCVHQRIEIKDTKEALDKIEEEQNK-SKKKA	no	Vaccine	rat (IgG)
		Vaccine *Vector/Type:* infected-cell lysate *Strain:* IIIB *HIV component:* virus **References** Shang1991, Maksiutov2002 • 12G-H1c7: Bound to 30-mer, but not to internal peptides – did not bind live infected cells – antigenic domain known as HPG30 [Shang1991] • 12G-H1c7: This epitope is similar to a fragment of the human protein CD40 ligand TNF-related activation protein (T-cell antigen GP39) (CD154), LDKIEDERN, as well as to a fragment of Lens-epithelium-derived growth factor, DIITEEDKSKKKGQ [Maksiutov2002].					
22	12I-D12g2	p17 (86–115)	p17 (86–115)	YCVHQRIEIKDTKEALDKIEEEQNK-SKKKA	no	Vaccine	rat (IgG2a)
		Vaccine *Vector/Type:* infected-cell lysate *Strain:* IIIB *HIV component:* virus **References** Shang1991, Maksiutov2002 • 12I-D12g2: Bound to 30-mer, but not to internal peptides – did not bind live infected cells – antigenic domain known as HPG30 [Shang1991] • 12I-D12g2: This epitope is similar to a fragment of the human protein CD40 ligand TNF-related activation protein (T-cell antigen GP39) (CD154), LDKIEDERN, as well as to a fragment of Lens-epithelium-derived growth factor, DIITEEDKSKKKGQ [Maksiutov2002].					
23	polyclonal	p17 (86–115)	p17 (86–115)	YSVHQRIDVKDTKEALEKIEEEQNK-SKKKA	L	Vaccine	murine (IgA)
		Vaccine *Vector/Type:* peptide *HIV component:* p17 *Adjuvant:* cholera toxin adjuvant **References** Bukawa1995 • Polyclonal secretory IgA antibody raised by oral mucosal immunization is able to neutralize IIIB, SF2, and MN – HIV-1 neutralization may be due to the V3, CD4 or HPG30 component of the multicomponent peptide immunogen [Bukawa1995]					
24	11H9	p17 (101–115)	p17 (101–115 SF2)	LEKIEEEQNKSKKKA?		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* inactivated virus *Strain:* CBL-1 *HIV component:* virus **Donor** R. B. Ferns and R. S. Tedder **References** Ferns1987, Ferns1989, Maksiutov2002 • 11H9: Reactive against p18 and p55 [Ferns1987] • 11H9: This epitope is similar to a fragment of Lens-epithelium-derived growth factor, DIITEEDKSKKKGQ [Maksiutov2002] • 11H9: UK Medical Research Council AIDS reagent: ARP344					
25	3-H-7 (3H7)	p17 (113–122)	p17 (113–122 BH10)	KKAQQAAADT	L	Vaccine	murine (IgG)
		Vaccine *Strain:* IIIB					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Niedrig1989, Robert-Hebmann1992b, Robert-Hebmann1992a, Levin1997 • 3-H-7: No cross-reactivity with HIV-2 ROD or SIV MAC by immunoblot [Niedrig1989] • 3-H-7: Called 3H7 – using a bicistronic vector, an intracellular Fab intrabody, 3H7, can inhibit HIV-1 infection when expressed in the cytoplasm of dividing CD4+ T cells – HXBIIIB and SI primary isolate virions from 3H7 expressing cells were far less infectious – 3H7 intrabody acts both at the stage of nuclear import and virus particle assembly [Levin1997]					
26	C5126	p17 (113–122)	p17 (113–122 HXB2)	KKAQQAAADT	no	Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* viral lysate *HIV component:* virus **References** Hinkula1990 • C5126: Defined epitope by peptide blocking of binding to native protein – WB reactive with p53 and p17 [Hinkula1990]					
27	1D9	p17 (119–132)	p17 (121–134 SF2)	AAGTGNSSQVSQNY		Vaccine	murine (IgG2a)
		Vaccine *Vector/Type:* inactivated virus *Strain:* CBL-1 *HIV component:* virus **Donor** R. B. Ferns and R. S. Tedder **References** Ferns1987, Ferns1989 • 1D9: Reactive against p18, but not p55 [Ferns1987] • 1D9: UK Medical Research Council AIDS reagent: ARP316					
28	4C9	p17 (119–132)	p18 (121–134 SF2)	AAGTGNSSQVSQNY		Vaccine	murine (IgG2a)
		Vaccine *Vector/Type:* inactivated virus *Strain:* CBL-1 *HIV component:* virus **Donor** R. B. Ferns and R. S. Tedder **References** Ferns1987, Ferns1989 • 4C9: Reactive against p18, but not p55 [Ferns1987] • 4C9: UK Medical Research Council AIDS reagent: ARP342					
29	4H2B1	p17 (119–132)	p17 (121–134 SF2)	AAGTGNSSQVSQNY			murine (IgG1)
		Donor R. B. Ferns and R. S. Tedder **References** Ferns1987, Ferns1989 • 4H2B1: Reactive against p18 and p55 of multiple isolates [Ferns1987] • 4H2B1: UK Medical Research Council AIDS reagent: ARP315					
30	9G5	p17 (119–132)	p17 (121–134 SF2)	AAGTGNSSQVSQNY		Vaccine	murine (IgM)
		Vaccine *Vector/Type:* inactivated virus *Strain:* CBL-1 *HIV component:* virus **Donor** R. B. Ferns and R. S. Tedder **References** Ferns1987, Ferns1989 • 9G5: Reactive against p18, but not p55 [Ferns1987] • 9G5: UK Medical Research Council AIDS reagent: ARP343					
31	15-21	p17 (121–132)	p17 (121–132 BRU)	DTGHSSQVSQNY	no	Vaccine	murine (IgG)
		Vaccine *Strain:* BRU **References** Robert-Hebmann1992b, Robert-Hebmann1992a					
32	31-11	p17 (121–132)	p17 (121–132 BRU)	DTGHSSQVSQNY	no	Vaccine	murine (IgG)
		Vaccine *Strain:* BRU **References** Robert-Hebmann1992b, Robert-Hebmann1992a					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
33	sc-FV p17	p17 (121–132)	p17 (121–132 BRU)	DTGHSSQVSQNY	L	Vaccine	murine (IgG1κ)
	Vaccine *Strain:* BRU **Ab type** C-term **Donor** Paul Zhou, NIH, Bethesda, MD, USA **References** Robert-Hebmann1992a, Tewari1998 • A single chain Ab (sc-FV) was made from an anti-p17 MAb, and intracellular binding of sc-FV resulted in inhibition of viral replication that was more pronounced when the sc-FV was expressed in the cytoplasm instead of the nucleus [Tewari1998]						
34	HyHIV-15	p17 (122–115)	p17 (87–115 JMH1)	SVHQRIDVKDTKEALEKIEEEQNKS-KKKA?	L	Vaccine	murine (IgG1)
	Vaccine *Vector/Type:* recombinant protein *HIV component:* p17 **References** Liu1995, Ota1998a • HyHIV-15: epitope uncertain, based on the best estimate from JMH1 sequence – Ka is 1.4 x 107 M-1 for rec p17 – stains the surface of infected cells indicating the antigen is exposed at the cell surface – inhibited growth of HIV-1 JMH1 in MT-4 cells when added 24 hours after the initial culture [Ota1998a]						

IV-C-2 p24 Antibodies

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
35	3A6	p24 (1–17)	p24 (122–149 BH10)	TGHSSQVSQNYPIVQNIQGQMVHQA-ISP	no	HIV-1 infection	human (IgG1κ)
		References Buchacher1992, Buchacher1994					
		• 3A6: The reactive peptide spans the p17/p24 border of gag [Buchacher1994]					
		• 3A6: Human MAbs against HIV generated by electrofusion of PBL from HIV-1 positive volunteers with CB-F7 cells [Buchacher1994]					
36	111/182	p24 (1–20)	p24 (134–153 IIIB)	PIVQNIQGQMVHQAISPRTL	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* beta-galactosidase fusion protein *Strain:* IIIB *HIV component:* p24					
		References Niedrig1991					
		• 111/182: Test specific evidence of cross-reactivity between HIV-1, HIV-2 and SIV MAC [Niedrig1991]					
37	112/021	p24 (1–20)	p24 (134–153 IIIB)	PIVQNIQGQMVHQAISPRTL	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* beta-galactosidase fusion protein *Strain:* IIIB *HIV component:* p24					
		References Niedrig1991					
		• 112/021: Test specific evidence of cross-reactivity between HIV-1, HIV-2 and SIV MAC [Niedrig1991]					
38	112/047	p24 (1–20)	p24 (134–153 IIIB)	PIVQNIQGQMVHQAISPRTL	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* beta-galactosidase fusion protein *Strain:* IIIB *HIV component:* p24					
		References Niedrig1991					
		• 112/047: Test specific evidence of cross-reactivity between HIV-1, HIV-2 and SIV MAC [Niedrig1991]					
39	ID8F6	p24 (11–25)	p24 (143–157 BRU)	VHQAISPRTLNAWVK	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* inactivated virus *Strain:* CBL-1 *HIV component:* virus					
		Donor R. B. Ferns and R. S. Tedder					
		References Ferns1987, Ferns1989					
		• ID8F6: Reacted with both p55 and p24 – showed less than 75% homologous inhibition [Ferns1987]					
		• ID8F6: UK Medical Research Council AIDS reagent: ARP348					
40	F5-2	p24 (14–23)	p24 (14–23 HXB2)	AISPRTLNAW	no		murine
		References Kusk1988, Kusk1992					
		• F5-2: In HIV-1+ individuals, antibody to AISPRTLNAW is associated with CD4 T-cell decline [Kusk1988, Kusk1992]					
41	CB-13/5 (CB-mab-p24/13-15)	p24 (21–25)	p24 (152–156)	NAWVK	no		murine (IgG1κ)
		References Grunow1990, Franke1992, Kuttner1992, Glaser1996					
		• CB-13/5: It is not clear whether the MAbs CD-13/5 and CB-mab-p24/13-15 are the same, but from the shared references in the primary articles they seem to be (database note)					
		• CB-13/5: Called CB-mab-p24/13-15 – the VDJ H and VJ L regions of CB-mab-p24/13-15 were sequenced [Kuttner1992]					
		• CB-13/5: Inhibits spread of HIV-1 in cell cultures [Franke1992]					
		• CB-13/5: Epitope described as VHQAISPRTLNAWVK – binding not affected by bound MAb CB-4/1 [Glaser1996]					
42	polyclonal	p24 (44–60)	p24 (176–192 LAI)	SEGATPQDLNTMLNTVG	no	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* recombinant protein, virus-like particle *Strain:* LAI *HIV component:* p24, p17, p55 *Adjuvant:* Freund's adjuvant					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Truong1997					
		• An ELISA assay was used to study a panel of Gag peptides – mature p24 CA epitopes mapped to residues 176-192, 201-218, 233-253, 285-304, and were recognized by antibodies elicited by rp24CA – one p17MA epitope, residues 11-25, and one p24CA epitope, residues 176-192, were recognized by antibodies raised against anti-p55 virus-like particles, suggesting a different antigenic properties for p24CA and p17MA antibodies depending on whether they are produced against the mature soluble protein or the immature assembled form of the gag proteins [Truong1997]					
43	3D3	p24 (45–50)	p24 (177–182 LAI)	EGATPQ		Vaccine	murine (IgG2b)
		Vaccine *Vector/Type:* inactivated virus *Strain:* CBL-1 *HIV component:* virus **Donor** R. B. Ferns and R. S. Tedder **References** Ferns1987, Ferns1989					
		• 3D3: Most broadly reactive of all the antibodies in this study[Ferns1987] • 3D3: UK Medical Research Council AIDS reagent: ARP314					
44	CD-4/1 (CB-4/1/1/F6)	p24 (46–56)	p24 (182–197)	GATPQDLNTML	no	Vaccine	murine (IgG2aκ)
		Vaccine *Vector/Type:* beta-galactosidase fusion protein *HIV component:* p24 **References** Grunow1990, Franke1992, Hohne1993, Glaser1996, Ehrhard1996					
		• CD-4/1: Inhibits spread of HIV-1 in cell cultures [Franke1992] • CD-4/1: Affinity of CB-4/1 to native p24 is lower than to peptide or denatured p24 – proposed that the peptide binds in a loop conformation [Hohne1993] • CD-4/1: Unusual p24-MAb binding kinetics, with biphasic association – probably due to conformational changes in p24, not to p24 dimerization [Glaser1996] • CD-4/1: Modification of p24 lysine residues by maleic anhydrid increased the affinity of CD-4/1, presumably due to conformational changes exposing a cryptic epitope [Ehrhard1996]					
45	15F8C7	p24 (47–56)	p24 (183–197)	ATPQDLNTML	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* purified HIV-1 **References** Janvier1990, Janvier1992					
		• 15F8C7: Mapped to aa209-217 through Pepscan method – cross-reacts with HIV-2 [Janvier1990] – maps to aa203-217 through EIA pentadecapeptide [Janvier1992]					
46	111/052	p24 (51–60)	p24 (183–192 IIIB)	DLNTMLNTVG	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* beta-galactosidase fusion protein *Strain:* IIIB *HIV component:* p24 **References** Niedrig1991					
		• 111/052: Weak cross-reaction with HIV-2 on WB, otherwise not cross-reactive with HIV-2 or SIV MAC [Niedrig1991]					
47	polyclonal	p24 (51–82)	Gag (183–214 LAI)	DLNTMLNTVGGHQAAMQMLKETINE-EAAEWDR	no	Vaccine	human (IgG)
		Vaccine *Vector/Type:* lipopeptide *Strain:* LAI *HIV component:* p24 *Adjuvant:* QS21 **References** Pialoux2001					
		• 28 subjects were vaccinated with six HIV-1 peptides that were selected to be particularly rich in CTL epitopes, presented in lipopeptides with or without adjuvant QS21 – HIV-specific Ab responses were detected in 25/28 (89%), proliferative in 19/28 (79%), and CTL in 13/24 (54%) of testable volunteers – only 4/28 had Ab responses to peptide G1, 4/28 had proliferative responses, and no patient had a CTL response [Pialoux2001]					
48	91-5	p24 (64–75)	p24 (196–207)	AAMQMLKETINE	no	HIV-1 infection	human (IgG1λ)
		References Gorny1989, Tyler1990, Robinson1990b, Gorny1998					
		• 91-5: Synthesized by immortalization of peripheral blood cells with Epstein-Barr virus [Gorny1989]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 91-5: Did not enhance HIV-1 IIIB infection [Robinson1990b] • 91-5: NIH AIDS Research and Reference Reagent Program: 1238					
49	1109/01	p24 (69–86)	p24 (201–218 BRU)	LKETINEEAAEWDRVHPV	no	Vaccine	murine (IgG)
		Vaccine *Strain:* IIIB *HIV component:* virus **References** Robert-Hebmann1992b, Robert-Hebmann1992a					
50	14D4E11	p24 (69–86)	p24 (201–218 BRU)	LKETINEEAAEWDRVHPV	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* purified HIV-1 **References** Janvier1990, Robert-Hebmann1992b, Robert-Hebmann1992a • 14D4E11: Mapped to aa209-217 through Pepscan method (original paper, AAEWDRVHP) – cross-reacts with HIV-2 [Janvier1990] and to aa203-217 through EIA pentadecapeptide [Janvier1992]					
51	1G5C8	p24 (69–86)	p24 (201–218 BRU)	LKETINEEAAEWDRVHPV	no	Vaccine	murine (IgG2b)
		Vaccine *Vector/Type:* protein *HIV component:* p24 **References** Janvier1990, Robert-Hebmann1992b, Robert-Hebmann1992a • 1G5C8: Mapped to aa209-217 through Pepscan method (original paper, AAEWDRVHP) [Janvier1990] and to aa203-217 through EIA pentadecapeptide [Janvier1992]					
52	47-2	p24 (69–86)	p24 (201–218 BRU)	LKETINEEAAEWDRVHPV	no	Vaccine	murine (IgG)
		Vaccine *Strain:* BRU **References** Robert-Hebmann1992b, Robert-Hebmann1992a					
53	714/01	p24 (69–86)	p24 (201–218 BRU)	LKETINEEAAEWDRVHPV	no	Vaccine	murine (IgG)
		Vaccine *Strain:* IIIB *HIV component:* virus **References** Robert-Hebmann1992b, Robert-Hebmann1992a					
54	polyclonal	p24 (69–86)	p24 (201–218 LAI)	LKETINEEAAEWDRVHPV	no	Vaccine	murine
		Vaccine *Vector/Type:* recombinant protein, virus-like particle *Strain:* LAI *HIV component:* p24, p17, p55 *Adjuvant:* Freund's adjuvant **References** Truong1997 • An ELISA assay was used to study a panel of Gag peptides – mature p24 CA epitopes mapped to residues 176-192, 201-218, 233-253, 285-304, and were recognized by antibodies elicited by rp24CA – one p17MA epitope, residues 11-25, and one p24CA epitope, residues 176-192, were recognized by antibodies raised against anti-p55 virus-like particles, suggesting a different antigenic properties for p24CA and p17MA antibodies depending on whether they are produced against the mature soluble protein or the immature assembled form of the gag proteins [Truong1997]					
55	111/073	p24 (71–81)	p24 (203–213 IIIB)	ETINEEAAEWD	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* beta-galactosidase fusion protein *Strain:* IIIB *HIV component:* p24 **References** Niedrig1991 • 111/073: cross-reactive between HIV-1, HIV-2 and SIV MAC by multiple assays [Niedrig1991]					
56	113/038	p24 (71–81)	p24 (203–213 IIIB)	ETINEEAAEWD	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* beta-galactosidase fusion protein *Strain:* IIIB *HIV component:* p24 **References** Niedrig1991 • 113/038: cross-reactive between HIV-1, HIV-2 and SIV MAC by multiple assays [Niedrig1991]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
57	1-E-4	p24 (71–85)	p24 (203–217)	ETINEEAAEWDRVHP	no	Vaccine	murine (IgG)
		Vaccine *Strain:* IIIB *HIV component:* virus					
		References Niedrig1989					
		• 1-E-4: One of nine MAbs that bind to this peptide [Niedrig1989]					
58	1-E-9	p24 (71–85)	p24 (203–217)	ETINEEAAEWDRVHP	no	Vaccine	murine (IgG)
		Vaccine *Strain:* IIIB *HIV component:* virus					
		References Niedrig1989					
		• 1-E-9: One of nine MAbs that bind to this peptide [Niedrig1989]					
59	10-E-7	p24 (71–85)	p24 (203–217)	ETINEEAAEWDRVHP	no	Vaccine	murine (IgG1)
		Vaccine *Strain:* IIIB *HIV component:* virus					
		References Niedrig1988, Niedrig1989					
		• 10-E-7: Cross reactive between HIV-1, HIV-2 and SIV [Niedrig1988]					
		• 10-E-7: One of nine MAbs that bind to this peptide – cross-reactive with HIV-2 ROD and SIV MAC [Niedrig1989]					
60	10-G-9	p24 (71–85)	p24 (203–217)	ETINEEAAEWDRVHP	no	Vaccine	murine (IgG1)
		Vaccine *Strain:* IIIB *HIV component:* virus					
		References Niedrig1988, Niedrig1989					
		• 10-G-9: HIV-1 specific [Niedrig1988]					
		• 10-G-9: One of nine MAbs that bind to this peptide [Niedrig1989]					
61	11-C-5	p24 (71–85)	p24 (203–217)	ETINEEAAEWDRVHP	no	Vaccine	murine (IgG1)
		Vaccine *Strain:* IIIB *HIV component:* virus					
		References Niedrig1988, Niedrig1989					
		• 11-C-5: HIV-1 specific [Niedrig1988]					
		• 11-C-5: One of nine MAbs that bind to this peptide [Niedrig1989]					
62	2-E-4	p24 (71–85)	p24 (203–217)	ETINEEAAEWDRVHP	no	Vaccine	murine (IgG2a)
		Vaccine *Strain:* IIIB *HIV component:* virus					
		References Niedrig1988, Niedrig1989					
		• 2-E-4: Cross reactive between HIV-1, HIV-2 and SIV by ELISA, HIV-1 and HIV-2 by WB [Niedrig1988]					
		• 2-E-4: One of nine MAbs that bind to this peptide – cross-reactive with HIV-2 ROD [Niedrig1989]					
63	2-H-4	p24 (71–85)	p24 (203–217)	ETINEEAAEWDRVHP	no	Vaccine	murine (IgG1)
		Vaccine *Strain:* IIIB *HIV component:* virus					
		References Niedrig1988, Niedrig1989					
		• 2-H-4: Cross reactive between HIV-1, HIV-2 and SIV by ELISA, HIV-1 and HIV-2 by WB [Niedrig1988]					
		• 2-H-4: One of nine MAbs that bind to this peptide – cross-reactive with HIV-2 ROD [Niedrig1989]					
64	8-D-2	p24 (71–85)	p24 (203–217)	ETINEEAAEWDRVHP	no	Vaccine	murine (IgG2a)
		Vaccine *Strain:* IIIB *HIV component:* virus					
		References Niedrig1989, Robert-Hebmann1992b, Robert-Hebmann1992a					
		• 8-D-2: HIV-1 specific [Niedrig1988]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 8-D-2: One of nine MAbs that bind to this peptide [Niedrig1989]					
65	8-G-9	p24 (71–85)	p24 (203–217)	ETINEEAAEWDRVHP	no	Vaccine	murine (IgG)
		Vaccine *Strain:* IIIB *HIV component:* virus **References** Niedrig1989 • 8-G-9: One of nine MAbs that bind to this peptide [Niedrig1989]					
66	8-H-7	p24 (71–85)	p24 (203–217)	ETINEEAAEWDRVHP	no	Vaccine	murine (IgG3)
		Vaccine *Strain:* IIIB *HIV component:* virus **References** Niedrig1988, Niedrig1989, Robert-Hebmann1992b, Robert-Hebmann1992a • 8-H-7: One of nine MAbs that bind to this peptide [Niedrig1989]					
67	C5123	p24 (71–85)	p24 (203–217 HXB2)	ETINEEAAEWDRVHP	no	Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* viral lysate *HIV component:* virus **References** Hinkula1990 • C5123: Epitope defined by peptide blocking of binding to native protein – WB reactive with p53 and p24 [Hinkula1990]					
68	1-B-7	p24 (76–85)	p24 (208–217 BH10)	EAAEWDRVHP	no	Vaccine	murine (IgG1)
		Vaccine *Strain:* IIIB **References** Niedrig1988, Niedrig1989 • 1-B-7: Reacts with two overlapping peptides, region of overlap is given – reacted with HIV-2 and SIV MAC [Niedrig1989]					
69	3-B-7	p24 (76–85)	p24 (208–217 BH10)	EAAEWDRVHP	no	Vaccine	murine (IgG1)
		Vaccine *Strain:* IIIB **References** Niedrig1988, Niedrig1989 • 3-B-7: Reacts with two overlapping peptides, region of overlap is given – reacted with HIV-2 [Niedrig1989]					
70	6-D-12	p24 (76–85)	p24 (208–217 BH10)	EAAEWDRVHP	no	Vaccine	murine (IgG1)
		Vaccine *Strain:* IIIB **References** Niedrig1988, Niedrig1989 • 6-D-12: Reacts with two overlapping peptides, region of overlap is given – reacted with HIV-2 [Niedrig1989]					
71	6-E-7	p24 (76–85)	p24 (208–217 BH10)	EAAEWDRVHP	no	Vaccine	murine (IgG1)
		Vaccine *Strain:* IIIB **References** Niedrig1988, Niedrig1989 • 6-E-7: Reacts with two overlapping peptides, region of overlap is given – reacted with HIV-2 and SIV MAC [Niedrig1989]					
72	8-D-5	p24 (76–85)	p24 (208–217 BH10)	EAAEWDRVHP	no	Vaccine	murine (IgG)
		Vaccine *Strain:* IIIB **References** Niedrig1988, Niedrig1989 • 8-D-5: Reacts with two overlapping peptides, region of overlap is given – bound only HIV-1 [Niedrig1989]					
73	FF1	p24 (76–90)	p24 (208–222 HXB2)	EAAEWDRVHPVHAGP	no	Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* inactivated virus **References** Hinkula1990 • FF1: Epitope defined by peptide blocking of binding to native protein – WB reactive with p53 and p24 [Hinkula1990]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
74	113/072	p24 (81–90)	p24 (213–222 IIIB)	DRVHPVHAGP	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* beta-galactosidase fusion protein *Strain:* IIIB *HIV component:* p24 **References** Niedrig1991 • 113/072: Weak cross-reaction with HIV-2 on WB, otherwise not cross-reactive with HIV-2 or SIV MAC [Niedrig1991]					
75	25.3	p24 (82–102)	p24 (82–102)	RVHPVHAGPIAPGQMREPRGS	no		murine (IgG1κ)
		References Momany1996 • 25.3: Crystal structure of the CA protein bound to Fab 25.3 was solved – monomers form 7 alpha-helices arranged in a coiled-coil – Fab binds to a long antigenic peptide that separates the longest helices, with a salt bridge at CA 82 R, and interactions as far away as positions 100 and 102 [Momany1996]					
76	13-102-100	p24 (84–94)	p24 (102–112 IIIB)	HPVHAGPIAPG			murine (IgG)
		Donor Advanced Technologies, Inc., Columbia, MD **References** Parker1996, Qian1998 • 13-102-100: Binding site (HPVHAGPIAPG) defined by epitope footprinting – first binding p24 to MAb, then allowing proteolytic cleavage to take place to cleave unprotected residues, then performing mass spectrometry to identify protected residues of epitope [Parker1996] • 13-102-100: Affinity capillary electrophoresis was used to fine map this epitope, and the optimal peptide was defined as VHAGPIAPGIAP – this method uses migration time shifts to probe relative affinities of Abs – the antibody binds to the cyclophilin A binding domain [Qian1998]					
77	RL4.72.1	p24 (87–101)	p24 (219–233 BRU)	HAGPIAPGQMREPRG	no	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* inactivated virus *Strain:* clade D strain NDK *HIV component:* virus **References** Tatsumi1990, Robert-Hebmann1992b, Robert-Hebmann1992a • RL4.72.1: Immunized with inactivated HIV NDK, D clade, reacts with B clade peptide [Robert-Hebmann1992a]					
78	406/01	p24 (101–121)	p24 (233–253 BRU)	GSDIAGTTSTLQEQIGWMTNN	no	Vaccine	murine (IgG)
		Vaccine *Strain:* IIIB **References** Robert-Hebmann1992b, Robert-Hebmann1992a					
79	polyclonal	p24 (101–121)	p24 (233–253 LAI)	GSDIAGTTSTLQEQIGWMTNL	no	Vaccine	murine
		Vaccine *Vector/Type:* recombinant protein, virus-like particle *Strain:* LAI *HIV component:* p24, p17, p55 *Adjuvant:* Freund's adjuvant **References** Truong1997 • An ELISA assay was used to study a panel of Gag peptides – mature p24 CA epitopes mapped to residues 176-192, 201-218, 233-253, 285-304, and were recognized by antibodies elicited by rp24CA – one p17MA epitope, residues 11-25, and one p24CA epitope, residues 176-192, were recognized by antibodies raised against anti-p55 virus-like particles, suggesting a different antigenic properties for p24CA and p17MA antibodies depending on whether they are produced against the mature soluble protein or the immature assembled form of the gag proteins [Truong1997]					
80	38:9.6K (38:96K)	p24 (121–130)	p24 (253–262 HXB2)	NPPIPVGEIY	no	Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* p24-p15 **References** Hinkula1990 • 38:9.6K: Called 38:96K – epitope defined by peptide blocking of binding to native protein – WB reactive with p53 and p24 [Hinkula1990] • 38:9.6K: UK Medical Research Council AIDS reagent: ARP365					
81	EB1A9	p24 (121–135)	p24 (253–267 LAI)	NPPIPVGEIYKRWII		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* inactivated virus *Strain:* CBL-1 *HIV component:* virus **Donor** R. B. Ferns and R. S. Tedder **References** Ferns1987, Ferns1989					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• EB1A9: Reacted with both p55 and p24 – showed less than 75% homologous inhibition [Ferns1987] • EB1A9: UK Medical Research Council AIDS reagent: ARP345					
82	polyclonal	p24 (121–152)	Gag (253–284 LAI)	NPPIPVGEIYKRWIILGLNKIVRMY-SPTSILD	no	Vaccine	human (IgG)
		Vaccine *Vector/Type:* lipopeptide *Strain:* LAI *HIV component:* p24 *Adjuvant:* QS21 **References** Pialoux2001 • 28 subjects were vaccinated with six HIV-1 peptides that were selected to be particularly rich in CTL epitopes, presented in lipopeptides with or without adjuvant QS21 – HIV-specific Ab responses were detected in 25/28 (89%), proliferative in 19/28 (79%), and CTL in 13/24 (54%) of testable volunteers – 25/28 had Ab responses to peptide G2, 14/28 had proliferative responses, and CTL responses were detected [Pialoux2001]					
83	30:3E5	p24 (141–170)	p24 (273–302 HXB2)	IVRMYSPTSILDIRQGPKEPFRDYV-DRFYK		Vaccine	murine (IgG1λ)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* p24-p15 **Donor** B. Wahren **References** Hinkula1990 • 30:3E5: Epitope defined by peptide blocking of binding to native protein – WB reactive with p53 and p24 [Hinkula1990] • 30:3E5: UK Medical Research Council AIDS reagent: ARP367					
84	EF7	p24 (141–170)	p24 (273–302 HXB2)	IVRMYSPTSILDIRQGPKEPFRDYV-DRFYK		Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* p24-p15 **References** Hinkula1990, Lundin1996 • EF7: Epitope defined by peptide blocking of binding to native protein – WB reactive with p53 [Hinkula1990] • EF7: Included as a control [Lundin1996] • EF7: UK Medical Research Council AIDS reagent: ARP366					
85	LH-104-E	p24 (143–148)	p24 (275–280 BRU)	RMYSPT	no	Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* peptide *Strain:* BRU **References** Haaheim1991 • LH-104-E: Reacts with both p24 and p55 [Haaheim1991] • LH-104-E: UK Medical Research Council AIDS reagent: ARP319					
86	1B2C12	p24 (149–154)	p24 (273–292 IIIB)	SILDIR	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* purified HIV-1 **References** Janvier1990 • 1B2C12: Reacts with HIV-1 and HIV-2 – mapped to aa281-286 through Pepscan method [Janvier1990], and to aa273-292 through EIA pentadecapeptide method [Janvier1992]					
87	LH-104-K	p24 (149–154)	p24 (281–286 BRU)	SILDIR	no	Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* peptide *Strain:* BRU **References** Haaheim1991 • LH-104-K: Binds exclusively with p24 (not p55) [Haaheim1991] • LH-104-K: UK Medical Research Council AIDS reagent: ARP322					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
88	LH-104-A	p24 (152–157 + 219–224)	p24 (BRU)	DIRQGP+QGVGGP	no	Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* peptide *HIV component:* p24 **References** Haaheim1991 • LF-104-A: A 104 amino acid peptide was used to immunize mice – hexapeptide scans revealed two reactive p24 peptides – cross-competition studies indicated the region 270-286 [Haaheim1991] • LH-104-A: UK Medical Research Council AIDS reagent: ARP307					
89	1.17.3	p24 (152–172)	p24 (152–172 SIVmac)	CVKQGPKEPFQSYVDRFYKSL	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* inactivated virus *Strain:* AGM TYO-7 *HIV component:* virus **References** Otteken1992 • 1.17.3: Recognized an epitope present on HIV-2/SIVmac (MAC251/32H) and HIV-2smmH4, but not SIVagmTYO-1, HIV-1 IIIB or SIVmnd [Otteken1992]					
90	1A7	p24 (152–172)	p24 (152–172 SIVmac)	CVKQGPKEPFQSYVDRFYKSL	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* inactivated virus *Strain:* AGM TYO-7 *HIV component:* virus **References** Otteken1992 • 1A7: Recognized an epitope present on HIV-2/SIVmac (MAC251/32H) and HIV-2smmH4, but not SIVagmTYO-1, HIV-1 IIIB or SIVmnd [Otteken1992]					
91	1F6	p24 (152–172)	p24 (152–172 SIVmac)	CVKQGPKEPFQSYVDRFYKSL	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* inactivated virus *Strain:* AGM TYO-7 *HIV component:* virus **References** Otteken1992 • 1F6: Recognized an epitope present on HIV-2/SIVmac (MAC251/32H) and HIV-2smmH4, but not SIVagmTYO-1, HIV-1 IIIB or SIVmnd [Otteken1992]					
92	23A5G4	p24 (153–172)	p24 (285–304 IIIB)	IRQGPKEPFRDYVDRFYKTL	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* p24 **References** Janvier1990, Janvier1996 • 23A5G4: Mapped to aa209-217 through Pepscan method [Janvier1990] and to aa285-304 through EIA pentadecapeptide method [Janvier1992] • 23A5G4: A few sera which were able to bind the linear sequence 178-192, but not sequence 288-302 in an indirect peptide ELISA inhibited the binding of 23A5G4 to the native p24 [Janvier1996]					
93	23A5G5	p24 (153–172)	p24 (285–304 BRU)	IRQGPKEPFRDYVDRFYKTL	no	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* protein *Strain:* IIIB *HIV component:* p24 **References** Robert-Hebmann1992b, Robert-Hebmann1992a					
94	3D10G6	p24 (153–172)	p24 (285–304 IIIB)	IRQGPKEPFRDYVDRFYKTL	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* purified HIV-1 **References** Janvier1990 • 3D10G6: Epitope cross-reacts with HIV-1 and HIV-2 – mapped to aa260-267 through Pepscan method [Janvier1990] and to aa285-304 through EIA pentadecapeptide method [Janvier1992]					
95	polyclonal	p24 (153–172)	p24 (285–304 LAI)	IRQGPKEPFRDYVDRFYKTL	no	Vaccine	murine
		Vaccine *Vector/Type:* recombinant protein, virus-like particle *Strain:* LAI *HIV component:* p24, p17, p55 *Adjuvant:* Freund's adjuvant **References** Truong1997					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• An ELISA assay was used to study a panel of Gag peptides – mature p24 CA epitopes mapped to residues 176-192, 201-218, 233-253, 285-304, and were recognized by antibodies elicited by rp24CA – one p17MA epitope, residues 11-25, and one p24CA epitope, residues 176-192, were recognized by antibodies raised against anti-p55 virus-like particles, suggesting a different antigenic properties for p24CA and p17MA antibodies depending on whether they are produced against the mature soluble protein or the immature assembled form of the gag proteins [Truong1997]					
96	F5-4	p24 (153–175)	p24 (153–174 HXB2)	IRQGPKEPFRDYVDRFYKTLRAE	no		murine
		References Kusk1988, Kusk1992 • F5-4: Binds to a location in the most hydrophilic region of p24 [Kusk1988, Kusk1992]					
97	MO9.42.2	p24 (153–178)	p24 (285–310 BRU)	IRQGPKEPFRDYVDRFYKTLRAEQAS	no	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* virus *Strain:* HIV2 ROD *HIV component:* virus **References** Robert-Hebmann1992b, Robert-Hebmann1992a • MO9.42.2: Reacts with HIV-1s, HIV-2s, and SIVs in rec protein ELISA [Robert-Hebmann1992b]					
98	MO9.50.2	p24 (153–178)	p24 (285–310 BRU)	IRQGPKEPFRDYVDRFYKTLRAEQAS	no	Vaccine	murine (IgG)
		Vaccine *Strain:* HIV2 ROD **References** Robert-Hebmann1992b, Robert-Hebmann1992a • MO9.50.2: Reacts with HIV-1s, HIV-2s, and SIVs in rec protein ELISA [Robert-Hebmann1992b]					
99	V10	p24 (155–169)	p24 (289–303 IIIB)	QGPKEPFRDYVDRFY	no	virus	murine
		References Matsuo1992 • V10: Reacts with HIV-1 and SIV AGM analogous peptides [Matsuo1992]					
100	V107	p24 (155–177)	p24 (289–311 IIIB)	QGPKEPFRDYVDRFYKTLRAEQA	no	virus	murine
		References Matsuo1992 • V107: Reacts with FIV, HIV-1 and SIV AGM analogous peptides [Matsuo1992]					
101	LH-104-C	p24 (156–161 + 219–224)	p24 (BRU)	GPKEPF+QGVGGP	no	Vaccine	murine (IgG3κ)
		Vaccine *Vector/Type:* peptide *HIV component:* p24 **References** Haaheim1991 • LF-104-C: A 104 amino acid peptide was used to immunize mice – hexapeptide scans revealed two reactive p24 peptides – cross-competition studies indicated the region 351-373 [Haaheim1991] • LH-104-C: UK Medical Research Council AIDS reagent: ARP309					
102	12-B-4	p24 (161–170)	p24 (293–302 IIIB)	FRDYVDRFYK	no	Vaccine	murine (IgG1)
		Vaccine *Strain:* IIIB *HIV component:* virus **References** Niedrig1988, Niedrig1989 • 12-B-4: Epitope is defined as the overlap between two HIV-1 reactive peptides – cross-reacts with HIV-2 ROD and SIV MAC [Niedrig1988, Niedrig1989]					
103	C5122	p24 (161–170)	p24 (293–302 HXB2)	FRDYVDRFYK	no	Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* viral lysate *HIV component:* virus **References** Hinkula1990 • C5122: Defined by peptide blocking of binding to native protein – WB reactive with p53 and p24 [Hinkula1990]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
104	9A4C4	p24 (170–188)	p24 (303–317 IIIB)	KTLRAEQASQEVKNWMTET	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* IIIB *HIV component:* p24 **References** Janvier1990, Robert-Hebmann1992b, Robert-Hebmann1992a • 9A4C4: Mapped to aa260-267 through Pepscan method [Janvier1990] – and to aa303-317 through EIA pentadecapeptide method [Janvier1992]					
105	11C10B10	p24 (171–185)	p24 (303–317 IIIB)	TLRAEQASQEVKNWM	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* p24 **References** Janvier1990 • 11C10B10: Mapped to aa260-267 through Pepscan method [Janvier1990] and to aa303-317 through EIA pentadecapeptide method [Janvier1992]					
106	11D11F2	p24 (171–185)	p24 (303–317 IIIB)	TLRAEQASQEVKNWM	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* p24 **References** Janvier1990 • 11D11F2: Mapped to aa260-267 through Pepscan method [Janvier1990] and to aa303-317 through EIA pentadecapeptide method [Janvier1992]					
107	CD12B4	p24 (171–185)	p24 (303–317 LAI)	TLRAEQASQEVKNWM		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* inactivated virus *Strain:* CBL-1 *HIV component:* virus **Donor** R. B. Ferns and R. S. Tedder **References** Ferns1987, Ferns1989 • CD12B4: Reacted with both p55 and p24 – strain-specific binding [Ferns1987] • CD12B4: UK Medical Research Council AIDS reagent: ARP346					
108	BE3	p24 (176–190)	p24 (308–322 HXB2)	QASQEVKNWMTETLL	no	Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* p24-p15 **Donor** B. Wahren **References** Hinkula1990 • BE3: Defined by peptide blocking of binding to native protein – WB reactive with p53 and p24 [Hinkula1990] • BE3: UK Medical Research Council AIDS reagent: ARP368					
109	L14	p24 (176–190)	p24 (308–322 HXB2)	QASQEVKNWMTETLL	no	Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* p24-p15 **Donor** B. Wahren **References** Hinkula1990 • L14: Defined by peptide blocking of binding to native protein – WB reactive with p53 and p24 [Hinkula1990] • L14: UK Medical Research Council AIDS reagent: ARP369					
110	108/03	p24 (181–190)	p24 (313–322 IIIB)	VKNWMTETLL	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* beta-galactosidase fusion protein *Strain:* IIIB *HIV component:* p24 **References** Niedrig1991 • 108/03: Cross-reactive between HIV-1, HIV-2 and SIV MAC by multiple tests [Niedrig1991]					
111	110/015	p24 (181–190)	p24 (313–322 IIIB)	VKNWMTETLL	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* beta-galactosidase fusion protein *Strain:* IIIB *HIV component:* p24 **References** Niedrig1991					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 110/015: Cross-reactive between HIV-1, HIV-2 and SIV MAC by multiple tests [Niedrig1991]					
112	32:32K	p24 (199–222)	p24 (331–354 HXB2)	KTILKALGPAATLEEMMTACQGVG		Vaccine	murine (IgG1λ)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* p24-p15					
		References Hinkula1990					
		• 32:32K: Epitope defined by peptide blocking of binding to native protein – WB reactive with p53 and p24 [Hinkula1990]					
		• 32:32K: UK Medical Research Council AIDS reagent: ARP368					
113	C5200	p24 (199–222)	p24 (331–354 HXB2)	KTILKALGPAATLEEMMTACQGVG		Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* viral lysate					
		References Hinkula1990					
		• C5200: Epitope defined by peptide blocking of binding to native protein [Hinkula1990]					
114	FH2	p24 (201–215)	p24 (333–347 HXB2)	ILKALGPAATLEEMM	no	Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* p24-p15					
		References Hinkula1990					
		• FH2: Defined by peptide blocking of binding to native protein – WB reactive with p53 and p24 [Hinkula1990]					
115	13B5	p24 (205–214)	p24 (205–213)	LGPAATLEEM		Vaccine	murine
		Vaccine *Vector/Type:* recombinant protein *HIV component:* p24					
		Ab type C-term **Donor** bioMerieux					
		References Berthet-Colominas1999					
		• 13B5: Fab which was bound to p24 capsid for crystallization and study of p24's structure [Berthet-Colominas1999]					
116	106/01	p24 (211–230)	p24 (343–362 IIIB)	LEEMMTACQGVGGPGHKARV	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* beta-galactosidase fusion protein *Strain:* IIIB *HIV component:* p24					
		References Niedrig1991					
		• 106/01: Cross-reactive between HIV-1, HIV-2 and SIV MAC by multiple tests [Niedrig1991]					
117	LH-104-B	p24 (225–230)	p24 (357–362 BRU)	GHKARV	no	Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* peptide *Strain:* BRU					
		References Haaheim1991					
		• LH-104-B: Binds exclusively with p55 (not p24), in contrast to LH-104-I [Haaheim1991]					
		• LH-104-B: UK Medical Research Council AIDS reagent: ARP308					
118	LH-104-I	p24 (226–231)	p24 (358–363 BRU)	HKARVL	no	Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* peptide *Strain:* BRU					
		References Haaheim1991					
		• LH-104-I: Binds exclusively with p24 (not p55), in contrast to LH-104-B [Haaheim1991]					
		• LH-104-I: UK Medical Research Council AIDS reagent: ARP321					

IV-C-3 p24-p2p7p1p6 Antibodies

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
119	LH-104-G	p24-p2p7p1p6 (231–5)	p24 (363–368 BRU)	LAEAMS	no	Vaccine	murine (IgG1κ)

Vaccine *Vector/Type:* peptide *Strain:* BRU
References Haaheim1991

- LH-104-G: Reacts with both p24 and p55, in contrast to LH-104-I [Haaheim1991]
- LH-104-G: This epitope overlaps the p24-p2 cleavage site, database note
- LH-104-G: UK Medical Research Council AIDS reagent: ARP320

IV-C-4 p2p7p1p6 Antibodies

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
120	i5B11	p2p7p1p6 (19–28)	p7 (5–14)	NFRNQRKIVK	no	Vaccine	rat (IgG2a)
		Vaccine *Vector/Type:* protein *HIV component:* NCp7 **References** Otake1994, Tanchou1994, Tanchou1995 • i5B11: i5B11 and 15B11 may be two names for the same MAb • i5B11: Epitope mapped by ELISA and BIAcore – inhibits NCp7 primer tRNA binding [Tanchou1994] • i5B11: MAb reacts with NCp7, NCp15, and partially inhibits NCp7-tRNA interaction [Tanchou1995]					
121	EC6	p2p7p1p6 (45–54)	p15 (408–417 HXB2)	PRKKGCWKCG	no	Vaccine	murine (IgG2aκ)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* p24-p15 **References** Hinkula1990 • EC6: Epitope defined by peptide blocking of binding to native protein – WB reactive with p53 [Hinkula1990]					
122	M12	p2p7p1p6 (45–54)	p15 (408–417 HXB2)	PRKKGCWKCG	no	Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* p24-p15 **References** Hinkula1990 • M12: There is a p15 and a gp120 MAb both called M12 • M12: Epitope defined by peptide blocking of binding to native protein – WB reactive with p53 [Hinkula1990]					
123	DG8	p2p7p1p6 (66–81)	p7 (52–67)	RQANFLGKIWPSYKGR		Vaccine	murine
		Vaccine *Vector/Type:* protein *HIV component:* NCp7 **References** Tanchou1995 • DG8: Binds proximal to the second zinc-finger, inhibits NCp7-tRNA interaction [Tanchou1995]					
124	EB5	p2p7p1p6 (66–81)	p7 (52–67)	RQANFLGKIWPSYKGR		Vaccine	murine
		Vaccine *Vector/Type:* protein *HIV component:* NCp7 **References** Tanchou1995 • EB5: Binds proximal to the second zinc-finger – mutation at position 59 (Lys to Ser) results in 10-fold reduction in reactivity [Tanchou1995]					
125	HH3	p2p7p1p6 (66–81)	p7 (52–67)	RQANFLGKIWPSYKGR	no	Vaccine	murine (IgG2b)
		Vaccine *Vector/Type:* protein *HIV component:* NCp7 **References** Tanchou1994, Tanchou1995 • HH3: Epitopes mapped by ELISA and BIAcore – does not inhibit NCp7 primer tRNA binding [Tanchou1994] • HH3: Binds proximal to the second zinc-finger [Tanchou1995]					
126	AD2	p2p7p1p6 (78–86)	p7 (64–72)	YKGRPGNFL	no	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* NCp7 **References** Tanchou1995 • AD2: Binds at C term of NCp7 [Tanchou1995]					
127	CA5	p2p7p1p6 (78–86)	p7 (64–72)	YKGRPGNFL	no	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* NCp7 **References** Tanchou1995					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• CA5: Binds at C term of NCp7 [Tanchou1995]					
128	DF3	p2p7p1p6 (78–86)	p7 (64–72)	YKGRPGNFL	no	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* NCp7					
		References Tanchou1995					
		• DF3: Binds at C term of NCp7 [Tanchou1995]					
129	EC3	p2p7p1p6 (78–86)	p7 (64–72)	YKGRPGNFL	no	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* NCp7					
		References Tanchou1995					
		• EC3: Binds at C term of NCp7 [Tanchou1995]					
130	FC12	p2p7p1p6 (78–86)	p7 (64–72)	YKGRPGNFL	no	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* NCp7					
		References Tanchou1995					
		• FC12: Binds at C term of NCp7, reacts with NCp15, inhibits NCp7-tRNA interaction [Tanchou1995]					
131	GE4	p2p7p1p6 (78–86)	p7 (64–72)	YKGRPGNFL	no	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* NCp7					
		References Tanchou1995					
		• GE4: Binds at C term of NCp7 [Tanchou1995]					
132	JB7	p2p7p1p6 (78–86)	p7 (64–72)	YKGRPGNFL	no	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* NCp7					
		References Tanchou1995					
		• JB7: Binds at C term of NCp7 [Tanchou1995]					
133	JF11	p2p7p1p6 (78–86)	p7 (64–72)	YKGRPGNFL	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* NCp7					
		References Tanchou1994, Tanchou1995					
		• JF11: Epitopes mapped by ELISA and BIAcore – does not inhibit NCp7 primer tRNA binding [Tanchou1994]					
		• JF11: Binds at C term of NCp7 [Tanchou1995]					

IV-C-5 Gag Antibodies

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
134	16/4/2	Gag	p24		no	Vaccine	
		Vaccine *Vector/Type:* DNA with CMV, MCK, or CMV/MCK hybrid promotors					
		References Bojak2002					
		• 16/4/2: The ability of three different promoters to induce Gag specific immune responses was compared. The cytomegaliovirus (CMV) early gene promoter, which allows constitutive expression in different cells of host tissue, the tissue specific muscle creatine kinase (MCK) promoter, which may be restricted to differentiated, multinucleated myofibers and so safer, and a hybrid MCK/CMV promoter – intramuscular immunization of BALB/c mice utilizing the MCK promoter in combination with a codon optimized gag gene generated humoral (IgG1 (Th1) and IgG2a (Th2)) and CTL immune responses against HIV-1 Gag, however, the quantified immune parameters were clearly reduced as compared to CMV promotor-driven Gag expression [Bojak2002]					
135	183-H12-5C	Gag	p24		no		murine (IgG1)
		Donor Bruce Chesebro and Kathy Wehrly, Rocky Mountain Laboratories, Hamilton, Montana					
		References Chesebro1992, Toohey1995, Wehrly1997					
		• 183-H12-5C: Used as antigen capture reagent for p24 ELISA [Chesebro1992, Toohey1995]					
		• 183-H12-5C: Cross-reacts with HIV1 and HIV-2 p24, and SIV p27 [Wehrly1997]					
		• 183-H12-5C: NIH AIDS Research and Reference Reagent Program: 3537					
136	241-D	Gag	p24		no		human (IgG1λ)
		Donor Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)					
		References Gorny1989, Tyler1990, Robinson1991					
		• 241-D: An antibody by this name is available in the NIH AIDS Research and Reference Reagent Program, and they refer to the papers [Gorny1989, Tyler1990, Robinson1991], but no p24 MAb by this name is discussed in these papers					
		• 241-D: MH AIDS Research and Reference Reagent program: 1244					
137	2A6	Gag	p17				
		Donor A. O. Arthur, Frederick Cancer Research and Development Center, Frederick, MD					
		References Pincus1998					
		• 2A6: Part of a panel of 17 MAbs used as controls testing for the dual specificity of MAb G11H3 for both p17 and mycoplasma [Pincus1998]					
138	5E2.A3k	Gag	p24 (1–158 SF2)		no		murine (IgG1)
		Donor Biodesign International, Kennebunk, Maine, USA					
		References Hochleitner2000a					
		• 5E2.A3k: The Ab binding site was studied with epitope excision (protein is bound in native conformation to immobilized MAb, then digested with proteolytic enzymes) and extraction (protein is digested then allowed to react with Ab), followed by mass spectroscopy, as well as lysine modification – the epitope is discontinuous, but involves the highly conserved N-term proline, and the antibody recognizes SIVs and HIV-2 as well as HIV-1 p24 [Hochleitner2000a]					
139	71-31	Gag	p24		no		human (IgG1λ)
		References Gorny1989, Robinson1990b, Robinson1991, Spear1993, Gorny1997, Gorny1998, Bandres1998					
		• 71-31: Did not enhance HIV-1 IIIB infection [Robinson1990b]					
		• 71-31: No enhancing or neutralizing activity [Robinson1991]					
		• 71-31: Did not mediate deposition of complement component C3 on HIV infected cells [Spear1993]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 71-31: Included as a negative control in studies that demonstrate that CXCR4 can bind to gp120 in the absence of CD4-gp120 interactions, and that this binding can be enhanced by Env deglycosylation [Bandres1998] • 71-31: NIH AIDS Research and Reference Reagent Program: 530					
140	91-6	Gag	p24 (121–240 IIIB)		no	HIV-1 infection	human (IgG1λ)
		References Gorny1989, Robinson1990b • 91-6: No enhancing activity for HIV-1 IIIB [Robinson1990b] • 91-6: NIH AIDS Research and Reference Reagent Program: 1239					
141	98-4.3	Gag	p24		no	HIV-1 infection	human (IgG1λ)
		References Robinson1991 • 98-4.3: No enhancing or neutralizing activity [Robinson1991]					
142	98-4.9	Gag	p24		no	HIV-1 infection	murine (IgG3λ)
		References Gorny1989					
143	AC2	Gag	p7		no	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* NCp7 **References** Tanchou1995 • AC2: Binds NCp7 independent of Zn fingers, does not react with NCp15 [Tanchou1995]					
144	BC1071	Gag	p24		no	HIV-1 infection	murine
		Donor Aalto BioReagents **References** Schonning1999 • BC1071: The stoichiometry of MAb neutralization was tested and MAb BC1071 was used in this study for virion quantification [Schonning1999]					
145	BE10	Gag	p7		no	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* NCp7 **References** Tanchou1995 • BE10: Binding NCp7 requires Zn fingers, does not react with NCp15, inhibits NCp7-tRNA interaction [Tanchou1995]					
146	CD9	Gag	p7		no	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* NCp7 **References** Tanchou1995 • CD9: Binds NCp7 independent of Zn fingers, does not react with NCp15 [Tanchou1995]					
147	CH9B2	Gag	p17			Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* inactivated virus *Strain:* CBL-1 *HIV component:* virus **Donor** R. B. Ferns and R. S. Tedder **References** Ferns1987, Ferns1989 • CH9B2: Reactive against p18 and p55 [Ferns1987] • CH9B2: UK Medical Research Council AIDS reagent: ARP349					
148	ED8	Gag	p7		no	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* NCp7 **References** Tanchou1995					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• ED8: Binds NCp7 independent of Zn fingers, does not react with NCp15 [Tanchou1995]					
149	EH12E1	Gag	p24			Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* inactivated virus *Strain:* CBL-1 *HIV component:* virus **Donor** R. B. Ferns and R. S. Tedder **References** Ferns1987, Ferns1989 • EH12E1: Reacted with p55 and p24 in WB [Ferns1987] • EH12E1: UK Medical Research Council AIDS reagent: ARP313					
150	G11G1	Gag	p17				rat
		References Shang1991, Pincus1996 • G11G1: Immunotoxins were generated by linking Env MAbs to ricin A – immunotoxins mediated cell killing, but only if the antigen was expressed at the cell surface – ricin-G11G1 did not mediate cell killing [Pincus1996]					
151	G11H3	Gag	p17				
		References Shang1991, Pincus1998 • G11H3: This MAb is cross-reactive between p17 and mycoplasma – this antibody binds strain specifically to the variable lipoprotein (Vlp) F of M. hyorhinis, in the region of the carboxy-terminal repeat CGGSTPTPEQGNNQGGSTPTPEQGNSQVSK – the p17 epitope is discontinuous, but p17 and Vlp F share the tetrapeptide SQVS [Pincus1998]					
152	HyHIV-19	Gag	p17 (JMH1)		no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* p17 **References** Liu1995, Ota1998a • HyHIV-19: Does not react with p17 peptides – Ka is 3.7 x 106 M-1 for rec p17 – inhibited growth of HIV-1 JMH1 in MT-4 cells when added 24 hours after the initial culture [Ota1998a]					
153	IE8G2	Gag	p24			Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* inactivated virus *Strain:* CBL-1 *HIV component:* virus **Donor** R. B. Ferns and R. S. Tedder **References** Ferns1987, Ferns1989 • IE8G2: Reacted with both p55 and p24 – broadly reactive – showed less than 75% homologous inhibition [Ferns1987] • IE8G2: UK Medical Research Council AIDS reagent: ARP347					
154	V7-8	Gag	p24		no	HIV-1 infection	murine (IgG3κ)
		References Robinson1990b, Montefiori1991 • V7-8: Did not enhance HIV-1 IIIB infection [Robinson1990b] • V7-8: Reacted with HIV-1IIIB, RF, and MN [Montefiori1991] • V7-8: NIH AIDS Research and Reference Reagent Program: 381					
155	anti-p24	Gag	p24			Vaccine	murine (IgG)
		Vaccine *Vector/Type:* recombinant protein, virus-like particle *HIV component:* Gag, Pol, Nef, gp120 **Donor** Intracel Co **References** Buonaguro2001					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• anti-p24: HIV-1 pr55 gag-based virus-like particles (VLP) carrying Nef and Pol open reading frames, as well as gp120 of the clade A isolate 94UG018, were created using a Baculovirus expression system to package additional ORFS into the VLP – anti-V3 and anti-p24 Abs were used to assess the expression levels and Gag and gp120-TM were found to be expressed at comparable levels on the VLP [Buonaguro2001]					
156	human sera	Gag	p24			HIV-1 infection	human (IgG)
		References Binley1997b					
		• Retention of anti-Env antibodies and loss of anti-Gag antibodies during progression was studied, and suggested to be the result of the loss of T-cell help and the unique ability of Env to stimulate B cells even in a backdrop of declining CD4 cells, because of the ability of Env to bind to the CD4 molecule [Binley1997b]					
157	polyclonal	Gag	Gag (LAI)			Vaccine	murine
		Vaccine *Vector/Type:* DNA prime with recombinant protein boost *Strain:* LAI *HIV component:* Gag, Tat, Nef *Adjuvant:* IL18					
		References Billaut-Mulot2001					
		• DNA vaccinated BALB/c mice primed and boosted with a multiepitopic vaccine with IL18 showed lymphoproliferative and CTL responses – co-administration of IL18 increased T-cell responses but decreased anti-HIV Ab levels [Billaut-Mulot2001]					
158	polyclonal	Gag	p24		no	Vaccine	rat
		Vaccine *Vector/Type:* gp120 depleted whole killed virus *Strain:* HZ321 (subtype A env, subtype G gag) *HIV component:* whole virus *Adjuvant:* CpG, Freund's adjuvant					
		References Moss2000					
		• Lewis rats co-immunized with HIV-1 antigen in Freund's and with immunostimulatory sequences CpG stimulated increased IFNγ expressing CD4+ and CD8+ T cells and anti-p24 antibodies relative to antigen in Freund's without CpG [Moss2000]					
159	polyclonal	Gag	p24 (SF2)			Vaccine	murine
		Vaccine *Vector/Type:* recombinant protein *Strain:* SF2 *HIV component:* gp120, p24 *Adjuvant:* PLG+MF-59 microparticles					
		References O'Hagan2000					
		• Microparticles were used as an adjuvant for entrapped HIV-1 gp120 and induced strong serum IgG responses in mice – polylactide co-glycolide polymer (PLG) microparticles in combination with MF-59 had the highest Ab response and also induced p24 specific CTL [O'Hagan2000]					
160	polyclonal	Gag	Gag (SF2)			Vaccine	murine, guinea pig, macaque
		Vaccine *Vector/Type:* DNA, recombinant protein *Strain:* SF2 *HIV component:* p55 *Adjuvant:* PLG microparticles, aluminum phosphate, MF-59					
		References O'Hagan2001					
		• DNA vaccines of codon-optimized Env and Gag genes driven by CMV promotors absorbed on to PLG microparticles were more effective than naked DNA at eliciting strong Ab responses (more rapid, higher titer, more stable), comparable to gp120 in MF-59 [O'Hagan2001]					
161	polyclonal	Gag	p24		no	Vaccine	rabbit (IgG)
		Vaccine *Vector/Type:* recombinant protein *Strain:* B subtype *HIV component:* p24					
		References Gupta2001					
		• Gag p24 is the mostly widely used HIV protein for serological based diagnostic kits — phage display libraries of HIV-1 p24 identified 2 epitope-rich regions: 70% of the clones that were identified using immunized rabbit sera had DNA fragments from the N-terminal region spanning 150–240 of Gag, and 30% from the carboxy-terminal region of p24 containing amino acids 310–360 — subtype B and C comparisons were made [Gupta2001]					
162	polyclonal	Gag	p55		no	Vaccine	murine
		Vaccine *Vector/Type:* recombinant protein, virus-like particle *Strain:* LAI *HIV component:* V3, CD4BS, p55					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Truong1996					
		• Antibodies raised against recombinant anti-p55 virus-like particles with the p24 region 196-226 deleted, bearing inserts of either the V3 or the CD4BS regions of gp120 were studied – no neutralizing responses, weak Env and strong Gag responses were elicited – the major homology region (MHR) and proximal sequences was found to be required for capsid assembly [Truong1996]					
163	polyclonal	Gag	p24 (LAI)			Vaccine	rabbit (IgG)
		Vaccine *Vector/Type:* virion, baculovirus and E. coli recombinant protein, peptides *Strain:* LAI *HIV component:* p24 *Adjuvant:* Freund's complete and incomplete adjuvant,					
		References Devito2000c					
		• To compare vaccine strategies, rabbits were immunized with virion HIV-1/Lai, baculovirus recombinant p24, E. coli recombinant p24-15, and p24-derived peptides – the rabbit immunized with peptides had the broadest linear epitope responses – the capture ELISA method using anti-p24 IgG preparations was shown to capture isolates from HIV-1 subtypes or clades A to G – only immunization with virion HIV-1/Lai and baculovirus recombinant p24 developed IgG that was capable of efficiently capturing HIV-1 p24 in ELISA producing Abs able to recognise native configurations [Devito2000c]					
164	polyclonal	Gag				Vaccine	murine
		Vaccine *Vector/Type:* DNA *Adjuvant:* CpG, phosphorothioate oligodeoxynucleotides (ODNs)					
		References Deml2001					
		• Immunization mice with a codon-optimized Gag was compared with a non-optimized Rev dependent Gag expression vector – Gag expression was at higher levels and Rev independent with the codon-optimized Gag, and i.m. immunization gave a stronger Th1-driven humoral and cellular immune response – intradermal immunization with either Gag DNA induced a Th2 response and no CTL [Deml2001]					
165	polyclonal	Gag			yes	HIV-1 infection	human
		References Montefiori2001					
		• In 7/9 patients in whom HAART was initiated during early seroconversion, NAbs to autologous strains were not found immediately following treatment interuption after 1-3 years, and Env and Gag Abs were low or undetected by ELISA indicating, that early HAART suppresses the normal antibody response to HIV-1, presumably by limiting the concentration of viral antigens needed to drive B-cell maturation – in 3 patients with a viral rebound autologous NAbs rapidly appeared and correlated with spontaneous down-regulation of viremia – prolonged control of viremia after stopping treatment persisted in the absence of detectable NAbs, suggesting that cellular immune responses alone can control viremia under certain circumstances – these results support the notion that virus-specific B-cell priming, combined with CD8+ CTL induction, may be beneficial for HIV-1 vaccines that aim to suppress viremia in the absence of complete protection to prevent disease and reduce the rate of virus transmission [Montefiori2001]					
166	polyclonal	Gag				Vaccine	murine (IgG)
		Vaccine *Vector/Type:* virus-like particle *HIV component:* Env, Gag *Adjuvant:* Freund's adjuvant					
		References Lebedev2000					
		• Virus-like particles (VLPs) in the form of spherical particles with yeast dsRNA enveloped in a polysaccharide matrix carrying the protein TBI, that contains fragments of HIV Env and Gag, were used to immunize BALB/c mice and induced specific Abs against HIV-1 as measured by ELISA with TBI [Lebedev2000]					
167	polyclonal	Gag			no	Vaccine	murine (IgG1, IgG2a)
		Vaccine *Vector/Type:* DNA with CMV, MCK, or CMV/MCK hybrid promotors					
		References Bojak2002					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• The ability of three different promoters to induce Gag specific immune responses was compared. The cytomegaliovirus (CMV) early gene promoter, which allows constitutive expression in different cells of host tissue, the tissue specific muscle creatine kinase (MCK) promoter, which may be restricted to differentiated, multinucleated myofibers and so safer, and a hybrid MCK/CMV promoter – intramuscular immunization of BALB/c mice utilizing the MCK promoter in combination with a codon optimized gag gene generated humoral (IgG1 (Th1) and IgG2a (Th2)) and CTL immune responses against HIV-1 Gag, however, the quantified immune parameters were clearly reduced as compared to CMV promotor-driven Gag expression [Bojak2002]					
168	polyclonal	Gag	p24		no	HIV-1 infection	human
		References Meles2002					
		• Indeterminant WB in Ethiopians: of 12,124 specimens blood specimens from Ethiopia, 1,437 (11.9%) were HIV-1-positive for antibody, and 91 (0.8%) gave equivocal results, most often due to p24 reactivity – subsequent testing confirmed many of the indeterminants were HIV-negative – the American Red Cross diagnostic criteria was more accurate than CDC or WHO, which would have given some false positive results [Meles2002]					
169	polyclonal HIVIG	Gag	p24		P	HIV-1 infection	human
		References Nichols2002					
		• NYBC-HIVIG derived from patients with high NAb titers and NABI-HIVIG derived from patients with high anti-p24 Ab titers were compared in neutralizing assay against a panel of six primary isolates—both could neutralize all isolates tested but the NYBC-HIVIG dose required for 50% neutralization was of 3.2 fold lower, showing that the source plasmas influence the effective concentration of NAb present in HIVIG [Nichols2002].					

IV-C-6 Protease Antibodies

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
170	1696	Protease (1–7)	Protease (1–7 BH10)	PQIYLWQ		Vaccine	murine (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* Protease **Ab type** N-term **References** Lescar1999 • 1696: MAb binds to HIV-1 and HIV-2, putative epitopes are PQIYLWQ and PQFSLWK respectively – Pro1 is critical, QIYLWQR residues 2-8, does not compete - MAb disrupts catalytic activity – crystal structure of Fab at 3 A resolution reveals a deep cavity lined by acidic and hydrophobic residues – the binding region is located within the region required for dimerization and the Fab structure could serve as a basis for drug design targeting this region [Lescar1999]					
171	10E7	Protease (36–46)	Protease (38–45 HXB2)	MSLPGRWKPKM	no	Vaccine	hamster (IgG)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Protease **References** Croix1993, Bjorling1992 • 10E7: Immunodominant region of protease in Armenian hamster (but only weakly reactive in people, see: [Bjorling1992]) – peptide MSLPGRWKP blocks protease binding [Croix1993]					
172	F11.2.32	Protease (36–46)	Protease (36–46 BH10)	MSLPGRWKPKM		Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* BH10 *HIV component:* Protease **Ab type** flap region **References** Lescar1996, Lescar1997, Lescar1999 • F11.2.32: Binding leads to significant inhibition in proteolytic activity – crystal structure of Fab-peptide was determined to 2.2 A resolution – bound peptide shows no structural similarity to the corresponding segment in native protease suggesting binding may distort protein structure [Lescar1997] • F11.2.32: Distortion may occur in the flap region of the protein, important for regulating access of substrate to the catalytic site [Lescar1999]					
173	13E1	Protease (38–45)	Protease (38–45 HXB2)	LPGRWKPK	no	Vaccine	hamster (IgG)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Protease **References** Croix1993 • 13E1: Binds to MSLPGRWKPKM with sightly higher affinity [Croix1993]					
174	8B11	Protease (38–45)	Protease (38–45 HXB2)	LPGRWKPK	no	Vaccine	hamster (IgG)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Protease **References** Croix1993 • 8B11: Binds to MSLPGRWKPKM with sightly higher affinity [Croix1993]					
175	8C10	Protease (38–45)	Protease (38–45 HXB2)	LPGRWKPK	no	Vaccine	hamster (IgG)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Protease **References** Croix1993 • 8C10: Binds to MSLPGRWKPKM with sightly higher affinity [Croix1993]					
176	8G5	Protease (38–45)	Protease (38–45 HXB2)	LPGRWKPK	no	Vaccine	hamster (IgG)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Protease **References** Croix1993 • 8G5: Binds to MSLPGRWKPKM with sightly higher affinity [Croix1993]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

IV-C-7 RT Antibodies

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
177	1E8	RT (65–73)	RT (65–73)	KKDSTKWRK	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* RT *Adjuvant:* nitrocellulose **References** Wu1993, Gu1996 • 1E8: Inhibits RT activity, binding site overlaps with two AZT resistance mutations [Wu1993] • 1E8: Significantly inhibits DNA polymerase activity of RT by hindering binding of dNTPs – additive or synergistic RT inhibition with nevirapine and delavirdine [Gu1996]					
178	1.152 B3	RT (294–302)	RT (294–302)	PLTEEAELE	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* RT **References** Orvell1991 • 1.152 B3: Weakly positive by immunofluorescence – binding inhibits RT enzymatic activity [Orvell1991]					
179	1.158 E2	RT (294–302)	RT (294–302)	PLTEEAELE	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* RT **References** Orvell1991 • 1.158 E2: Negative by immunofluorescence – binding inhibits RT enzymatic activity [Orvell1991]					
180	31D6	RT (294–318)	RT (294–319)	PLTEEAELELAENREILKEPVHGVY	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* E. coli Trp fusion protein *HIV component:* RT **References** Szilvay1992 • 31D6: Strong inhibitor of RT, > 50% inhibition [Szilvay1992]					
181	31G8	RT (294–318)	RT (294–319)	PLTEEAELELAENREILKEPVHGVY	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* E. coli Trp fusion protein *HIV component:* RT **References** Szilvay1992 • 31G8: Weak inhibitor of RT, reactive by immunofluorescence [Szilvay1992]					
182	32E7	RT (294–318)	RT (294–319)	PLTEEAELELAENREILKEPVHGVY	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* E. coli Trp fusion protein *HIV component:* RT **References** Szilvay1992 • 32E7: Weak inhibitor of RT, reactive by immunofluorescence [Szilvay1992]					
183	33D5	RT (294–318)	RT (294–319)	PLTEEAELELAENREILKEPVHGVY	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* E. coli Trp fusion protein *HIV component:* RT **References** Szilvay1992 • 33D5: Weak inhibitor of RT, reactive by immunofluorescence [Szilvay1992]					
184	5B2	RT (294–318)	RT (294–319)	PLTEEAELELAENREILKEPVHGVY	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* E. coli Trp fusion protein *HIV component:* RT **References** Szilvay1992 • 5B2: There is an RT specific Ab [Szilvay1992] and a gp41 specific Ab [Tian2001] both called 5B2 • 5B2: Weak inhibitor of RT, reactive by immunofluorescence [Szilvay1992]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 5B2: UK Medical Research Council AIDS reagent: ARP3018					
185	polyclonal	RT (295–304)	RT (295–304 PV22)	LTEEAELELA	no	HIV-1 infection	human (IgG)
		References Grimison1995					
186	1.153 G10	RT (350–354)	RT (350–354)	KTGKY	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* RT					
		References Orvell1991					
187	RTMAb8	RT (376–383)	RT (532–539)	TTESIVIW	no	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* RT					
		References Tisdale1988, Ferns1991					
188	1D4A3	RT (384–387)	RT (540–543)	GKIP	no	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* RT					
		References Ferns1991					
189	RT6H	RT (384–387)	RT (540–543)	GKIP	no	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* RT					
		References Ferns1991					
190	1.160 B3	RT (442–450)	RT (442–450)	VDGAANRET	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* RT					
		References Orvell1991					
191	polyclonal	RT (521–531)	RT (521–531 PV22)	IIEQLIKKEKV	no	HIV-1 infection	human (IgG)
		References Grimison1995					
192	C2003	RT (536–549)	RT (703–716 BH10)	VPAHKGIGGNEQVD	no	Vaccine	rabbit (IgG)
		Vaccine *Vector/Type:* peptide *Strain:* BH10					
		References DeVico1991					
		• C2003: Inhibits polymerase activity from a variety of retroviruses – RT protected from inhibition by preincubation with template primer [DeVico1991]					
193	6B9	RT	RT (155–250)		yes	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* HXB2 *HIV component:* RT					
		Ab type palm domain					
		References Chiba1996, Chiba1997, Ohba2001					
		• 6B9: In contrast to MAb 7C4, which binds to the thumb region of RT, 6B9 binds to the palm subdomain and does not inhibit RT activity [Chiba1996]					
194	5F	RT	RT (252–335)		yes	Vaccine	murine
		Vaccine *Vector/Type:* vaccinia *Strain:* HXB2 *HIV component:* RT					
		Ab type thumb domain					
		References Ohba2001					
		• 5F: BALB/c mice were vaccinated with vaccinia carrying RT and a phage display library was produced and panned with RT – Fabs 5F and 5G were cloned, both recognizing an immunodominant neutralizing RT epitope in the region of the template primer-binding site in the thumb domain also recognized by MAb 7C4 – sequencing revealed the heavy chains and light chains of 7C4, 5G and 7C4 are related [Ohba2001]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
195	5G	RT	RT (252–335)		yes	Vaccine	murine

Vaccine *Vector/Type:* vaccinia *Strain:* HXB2 *HIV component:* RT
Ab type thumb domain
References Ohba2001

- 5G: BALB/c mice were vaccinated with vaccinia carrying RT and a phage display library was produced and panned with RT – Fabs 5F and 5G were cloned, both recognizing an immunodominant neutralizing RT epitope in the region of the template primer-binding site in the thumb domain also recognized by MAb 7C4 – sequencing revealed the heavy chains and light chains of 7C4, 5G and 7C4 are related [Ohba2001]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
196	7C4	RT	RT (252–335)		yes	Vaccine	murine (IgG2a)

Vaccine *Vector/Type:* vaccinia *Strain:* HXB2 *HIV component:* RT
Ab type thumb domain
References Chiba1996, Chiba1997, Ohba2001

- 7C4: 7C4 was produced from a hybridoma cell line derived from a BALB/c mouse repeatedly immunized with RT in a vaccinia construct, and was found to inhibit RT through binding to the template primer-binding site, a possible target for RT inhibitors [Chiba1996]
- 7C4: 7C4 inhibits RT from HIV-1 strains IIIB, Bru, and IMS-1 but not HIV-2 strains GH-1 and LAV-2, SIV MAC, nor SIV MND [Chiba1997]
- 7C4: Fabs 5F and 5G both recognize the same immunodominant neutralizing RT epitope in the region of the template primer-binding site in the thumb domain recognized by MAb 7C4 – sequencing revealed the heavy chains and light chains of 7C4, 5G and 7C4 are related [Ohba2001]

IV-C-8 Integrase Antibodies

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
197	1C4	Integrase (1–16)	Integrase (1–16 HXB2)	FLDGIDKAQDEHEKYH	no	Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* HXB2 *HIV component:* Integrase **Ab type** N-term **References** Haugan1995, Nilsen1996 • 1C4: MAb interferes with integrase binding to DNA [Haugan1995] • 1C4: One of a large set of MAbs that interact with the N-terminal part of integrase: 1C4, 2C11, 2E3, 3E11, 3F9, 5F8, 6G5, 7B6, 7C6 – these MAbs inhibit end processing and DNA joining, but had little effect on integration activities [Nilsen1996]					
198	2C11	Integrase (1–16)	Integrase (1–16 HXB2)	FLDGIDKAQDEHEKYH	no	Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* HXB2 *HIV component:* Integrase **Ab type** N-term **References** Nilsen1996 • 2C11: One of a large set of MAbs that interact with the N-terminal part of integrase: 1C4, 2C11, 2E3, 3E11, 3F9, 5F8, 6G5, 7B6, 7C6 – these MAbs inhibit end processing and DNA joining, but had little effect on integration activities [Nilsen1996]					
199	2E3	Integrase (1–16)	Integrase (1–16 HXB2)	FLDGIDKAQDEHEKYH	no	Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* HXB2 *HIV component:* Integrase **Ab type** N-term **References** Nilsen1996, Ovod1992 • 2E3: There are two MAbs called 2E3 – the other one binds to Nef [Ovod1992] • 2E3: One of a large set of MAbs that interact with the N-terminal part of integrase: 1C4, 2C11, 2E3, 3E11, 3F9, 5F8, 6G5, 7B6, 7C6 – these MAbs inhibit end processing and DNA joining, but had little effect on integration activities [Nilsen1996]					
200	3E11	Integrase (1–16)	Integrase (1–16 HXB2)	FLDGIDKAQDEHEKYH	no	Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* HXB2 *HIV component:* Integrase **Ab type** N-term **References** Otteken1992, Nilsen1996 • 3E11: There is another MAb with this ID that recognizes p17 [Otteken1992] • 3E11: Recognized an epitope present on HIV-2/SIVmac, SIVagm, HIV-1, and SIVmnd [Otteken1992] • 3E11: One of a large set of MAbs that interact with the N-terminal part of integrase: 1C4, 2C11, 2E3, 3E11, 3F9, 5F8, 6G5, 7B6, 7C6 – these MAbs inhibit end processing and DNA joining, but had little effect on integration activities [Nilsen1996]					
201	3F9	Integrase (1–16)	Integrase (1–16 HXB2)	FLDGIDKAQDEHEKYH	no	Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* HXB2 *HIV component:* Integrase **Ab type** N-term **References** Nilsen1996 • 3F9: One of a large set of MAbs that interact with the N-terminal part of integrase: 1C4, 2C11, 2E3, 3E11, 3F9, 5F8, 6G5, 7B6, 7C6 – these MAbs inhibit end processing and DNA joining, but had little effect on integration activities [Nilsen1996]					
202	5F8	Integrase (1–16)	Integrase (1–16 HXB2)	FLDGIDKAQDEHEKYH	no	Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* HXB2 *HIV component:* Integrase					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		Ab type N-term **References** Haugan1995, Nilsen1996 • 5F8: There is another MAb with this ID that recognizes and unknown protein in HIV [Pinter1995] • 5F8: MAb interferes with integrase binding to DNA [Haugan1995] • 5F8: One of a large set of MAbs that interact with the N-terminal part of integrase: 1C4, 2C11, 2E3, 3E11, 3F9, 5F8, 6G5, 7B6, 7C6 – these MAbs inhibit end processing and DNA joining, but had little effect on integration activities [Nilsen1996]					
203	6G5	Integrase (1–16)	Integrase (1–16 HXB2)	FLDGIDKAQDEHEKYH	no	Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* HXB2 *HIV component:* Integrase **Ab type** N-term **References** Nilsen1996 • 6G5: One of a large set of MAbs that interact with the N-terminal part of integrase: 1C4, 2C11, 2E3, 3E11, 3F9, 5F8, 6G5, 7B6, 7C6 – these MAbs inhibit end processing and DNA joining, but had little effect on integration activities [Nilsen1996]					
204	7B6	Integrase (1–16)	Integrase (1–16 HXB2)	FLDGIDKAQDEHEKYH	no	Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* HXB2 *HIV component:* Integrase **Ab type** N-term **References** Nilsen1996 • 7B6: One of a large set of MAbs that interact with the N-terminal part of integrase: 1C4, 2C11, 2E3, 3E11, 3F9, 5F8, 6G5, 7B6, 7C6 – these MAbs inhibit end processing and DNA joining, but had little effect on integration activities [Nilsen1996]					
205	7C6	Integrase (1–16)	Integrase (1–16 HXB2)	FLDGIDKAQDEHEKYH	no	Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* HXB2 *HIV component:* Integrase **Ab type** N-term **References** Nilsen1996 • 7C6: One of a large set of MAbs that interact with the N-terminal part of integrase: 1C4, 2C11, 2E3, 3E11, 3F9, 5F8, 6G5, 7B6, 7C6 – these MAbs inhibit end processing and DNA joining, but had little effect on integration activities [Nilsen1996]					
206	6C5	Integrase (17–38)	Integrase (17–38 HXB2)	SNWRAMASDFNLPPVVAKEIVA	no	Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* HXB2 *HIV component:* Integrase **Ab type** N-term **References** Haugan1995, Nilsen1996 • 6C5: MAb interferes with integrase binding to DNA [Haugan1995] • 6C5: This MAb inhibits end processing and DNA joining, but had little effect on integration activities [Nilsen1996]					
207	8G4	Integrase (22–31 + 82–101)	Integrase (12–42 HXB2)	MASDFNLPPV+GYIEAEVIPAETGQ-ETAYFI?	no	Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* HXB2 *HIV component:* Integrase **References** Haugan1995, Nilsen1996 • 8G4: This MAb reacted strongly with peptides IN(12-31) and IN(22-42), and less strongly with peptide IN(82-101) – it did not react with a deletion mutant of positions 17-38 – this MAb inhibits end processing and DNA joining, but had little effect on integration activities [Nilsen1996] • 8G4: MAb interferes with integrase binding to DNA [Haugan1995]					
208	17 (mAb17)	Integrase (25–35)	Integrase (25–35)	DFNLPPVVAKE	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Integrase					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Bizub-Bender1994, Levy-Mintz1996, Yi2000b • 17: BALBc mice were immunized with rec integrase, hybridomas expressing anti-integrase Abs were generated, and the antibodies characterized – the Zn finger motif is in the binding region – MAbs 14 and 17 form a competition group [Bizub-Bender1994] • 17: Used for the creation of single chain variable antibody fragments (SFvs) for internal cellular expression – neutralization of IN activity prior to integration, whether the Ab is expressed in the nucleolus or the cytoplasm – relative binding affinity to IN: 12 > 17 = 33 > 21 > 4 [Levy-Mintz1996] • 17: Epitope mapped to helix-turn-helix motif in the N-term domain of Integrase, positions 25-35 – Zn binding stabilizes the Integrase-mAb17complex – both MAb and Fab form of mAb17 inhibit Integrase activity – epitope region likely to be involved in protein-protein interaction [Yi2000b]				
209	4D6	Integrase (42–55)	Integrase (42–55 HXB2)	KCQLKGEAMHGQVD	no	Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* HXB2 *HIV component:* Integrase **Ab type** N-term **References** Haugan1995, Nilsen1996 • 4D6: MAb interferes with integrase binding to DNA [Haugan1995] • 4D6: This MAb inhibits end processing and DNA joining, and reduces reintegration activity [Nilsen1996]					
210	7-16 (7-19)	Integrase (50–159)	Integrase (50–159 HXB2)		no	Vaccine	murine (IgG2b)
		Vaccine *Vector/Type:* chimeric maltose binding protein (MBP) *Strain:* IIIB *HIV component:* Integrase **Ab type** Integrase catalytic core **Donor** Yoshihiro Kitamura, Div of Mol Genetics, Nat Inst of Infectious Diseases, Musashimurayama, Japan **References** Ishikawa1999 • 7-16: Binds to the central catalytic domain – the paper seems to sometimes call this antibody 7-16, sometimes 7-19, a possible typo [Ishikawa1999]					
211	4F6	Integrase (56–102)	Integrase (56–102 HXB2)	CSPGIWQLDCTHLEGKVILVAVHVA-SGYIEAEVIPAETGQETAYFLL	no	Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* HXB2 *HIV component:* Integrase **Ab type** Integrase catalytic core **References** Haugan1995, Nilsen1996 • 4F6: MAb binding had minimal effects on IN in vitro activities [Nilsen1996] • 4F6: MAb interferes with integrase binding to DNA [Haugan1995]					
212	anti-K159	Integrase (151–163)	Integrase (163–175)	VESMNKELKKIIG		Vaccine	rabbit (IgG)
		Vaccine *Vector/Type:* peptide *HIV component:* Integrase **References** Maroun1999, Maksiutov2002 • anti-K159: Both the peptide K159, SQGVVESMNKELKKIIGQVRDQAEHLKTA, and the Abs raised against this peptide inhibit Integrase activity – K159 was found to fulfill condition of minimal number of helical heptads to achieve the formation of a stable coiled-coil structure – Integrase is proposed to function as a dimer interacting in this region [Maroun1999] • anti-K159: This epitope is similar to a fragment of the human protein Apoptosis regulator BCL-W (KIAA0271), ESVNKEMEPLVGQV [Maksiutov2002]					
213	5D9	Integrase (186–250)	Integrase (186–250 HXB2)		no	Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* HXB2 *HIV component:* Integrase **Ab type** Integrase DNA binding domain **References** Nilsen1996 • 5D9: MAb binding had minimal effects on IN in vitro activities [Nilsen1996]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 5D9: While C-term and N-term anti-Integrase MAbs interfere with Integrase-DNA binding, 5D9 which binds more centrally, does not [Haugan1995]					
214	8-6	Integrase (211–227)	Integrase (211–227 HXB2)	KELQKQITKIQNFRVYY	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* chimeric maltose binding protein (MBP) *Strain:* IIIB *HIV component:* Integrase **Donor** Yoshihiro Kitamura, Div of Mol Genetics, Nat Inst of Infectious Diseases, Musashimurayama, Japan **References** Ishikawa1999 • 8-6: Antibody binds proximal to the DNA binding region [Ishikawa1999]					
215	19 (2-19, scAb2-19)	Integrase (228–236)	Integrase (228–236 LAI)	RDSRNPLWK	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Integrase **References** Bizub-Bender1994, Levy-Mintz1996, Kitamura1999 • 19: BALBc mice were immunized with rec integrase, hybridomas expressing anti-integrase Abs were generated, and the antibodies characterized – 19 has a low binding affinity [Bizub-Bender1994] • 19: Called 2-19, scAb2-19 is a single-chain Ab made from MAb 2-19 –acts intra-cellularly to block infection at low MOI by binding to integrase – scAb interfered with the folding of Gag-Pol polyprotein, the Ab did not affect viral production in LAI transfected cells, but the virus produced was less infectious – authors suggest that the epitope may be conformational [Kitamura1999]					
216	2-19	Integrase (228–236)	Integrase (228–236 HXB2)	RDSRNPLWK	no	Vaccine	murine (IgG2b)
		Vaccine *Vector/Type:* chimeric maltose binding protein (MBP) *Strain:* IIIB *HIV component:* Integrase **Ab type** Integrase DNA binding domain **Donor** Yoshihiro Kitamura, Div of Mol Genetics, Nat Inst of Infectious Diseases, Musashimurayama, Japan **References** Ishikawa1999 • 2-19: MAb inhibits RT-Integrase interaction, and the terminal cleavage and strand transfer functions of Integrase, but not the disintegration activity [Ishikawa1999]					
217	8-22	Integrase (237–252)	Integrase (237–252 HXB2)	GPAKLLWKGEGAVVIQ	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* chimeric maltose binding protein (MBP) *Strain:* IIIB *HIV component:* Integrase **Ab type** Integrase DNA binding domain **Donor** Yoshihiro Kitamura, Div of Mol Genetics, Nat Inst of Infectious Diseases, Musashimurayama, Japan **References** Ishikawa1999 • 8-22: MAb inhibits the terminal cleavage and strand transfer functions of Integrase, but not the disintegration activity [Ishikawa1999]					
218	4-20	Integrase (253–261)	Integrase (253–261 HXB2)	DNSDIKVVP	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* chimeric maltose binding protein (MBP) *Strain:* IIIB *HIV component:* Integrase **Ab type** Integrase DNA binding domain **Donor** Yoshihiro Kitamura, Div of Mol Genetics, Nat Inst of Infectious Diseases, Musashimurayama, Japan **References** Ishikawa1999 • 4-20: Inhibits the terminal cleavage and strand transfer functions of Integrase, but not the disintegration activity [Ishikawa1999]					
219	6-19	Integrase (262–270)	Integrase (261–270 HXB2)	RRKAKIIRD	no	Vaccine	murine (IgG2b)
		Vaccine *Vector/Type:* chimeric maltose binding protein (MBP) *Strain:* IIIB *HIV component:* Integrase **Ab type** Integrase DNA binding domain **Donor** Yoshihiro Kitamura, Div of Mol Genetics, Nat Inst of Infectious Diseases, Musashimurayama, Japan **References** Ishikawa1999					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 6-19: Inhibits the terminal cleavage and strand transfer functions of Integrase, but not the disintegration activity [Ishikawa1999]					
220	7C3	Integrase (262–271)	Integrase (262–271 HXB2)	RRKAKIIRDY	no	Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* HXB2 *HIV component:* Integrase **References** Haugan1995, Nilsen1996 • 7C3: MAb interferes with integrase binding to DNA [Haugan1995] • 7C3: A set of three MAbs recognize an epitope in this region, 7C3, 7F11, and 8E5 – all three HIV-1 MAbs cross-react with HIV-2 IN – these MAbs inhibit end-processing, DNA joining and reintegration, and had little effect on disintegration [Nilsen1996]					
221	7F11	Integrase (262–271)	Integrase (262–271 HXB2)	RRKAKIIRDY	no	Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* HXB2 *HIV component:* Integrase **References** Nilsen1996, Lasky1987 • 7F11: A set of three MAbs recognize an epitope in this region, 7C3, 7F11, and 8E5 – all three HIV-1 MAbs cross-react with HIV-2 IN – these MAbs inhibit end-processing, DNA joining and reintegration, and had little effect on disintegration [Nilsen1996] • 7F11: There is another MAb with this name that binds to gp120 [Lasky1987]					
222	8E5	Integrase (262–271)	Integrase (262–271 HXB2)	RRKAKIIRDY	no	Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* HXB2 *HIV component:* Integrase **References** Haugan1995, Nilsen1996 • 8E5: MAb interferes with integrase binding to DNA [Haugan1995] • 8E5: A set of three MAbs recognize an epitope in this region, 7C3, 7F11, and 8E5 – all three HIV-1 MAbs cross-react with HIV-2 IN – these MAbs inhibit end-processing, DNA joining and reintegration, and had little effect on disintegration [Nilsen1996]					
223	MAb 35	Integrase (264–273)	Integrase (264–273)	KAKIIRDYGK	no	Vaccine	murine (IgGκ)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Integrase **References** Barsov1996, Acel1998 • MAb 35: There appears to be two different IN Abs with similar names: MAb 35 and 35 [Barsov1996, Bizub-Bender1994] • MAb 35: Although MAb 35 does not inhibit HIV-1 IN, Fab 35 inhibits 3'-end processing, strand transfer and disintegration [Barsov1996] • MAb 35: Integrase was shown to have intrinsic DNA polymerase activity that can catalyze gap repair – MAb 35 inhibits this activity [Acel1998]					

IV-C-9 Pol Antibodies

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
224	12	Pol	Integrase (1–58)		no	Vaccine	murine (IgG2a)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Integrase **References** Bizub-Bender1994, Levy-Mintz1996 • 12: BALBc mice were immunized with rec integrase, hybridomas expressing anti-integrase Abs were generated, and the antibodies characterized – the Zn finger motif is in the binding region – MAbs 12, 13 and 35 form a competition group [Bizub-Bender1994] • 12: Used for the creation of single-chain variable antibody fragments (SFvs) for internal cellular expression – neutralization of IN activity prior to integration, whether the Ab is expressed in the nucleolus or the cytoplasm – relative binding affinity to IN: 12 > 17 = 33 > 21 > 4 [Levy-Mintz1996]				
225	13	Pol	Integrase (1–58)		no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Integrase **References** Bizub-Bender1994 • 13: BALBc mice were immunized with rec integrase, hybridomas expressing anti-integrase Abs were generated, and the antibodies characterized – the Zn finger motif is in the binding region – MAbs 12, 13 and 35 form a competition group [Bizub-Bender1994]				
226	14	Pol	Integrase (1–58)		no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Integrase **References** Bizub-Bender1994 • 14: BALBc mice were immunized with rec integrase, hybridomas expressing anti-integrase Abs were generated, and the antibodies characterized – the Zn finger motif is in the binding region – MAbs 14 and 17 form a competition group [Bizub-Bender1994]				
227	16	Pol	Integrase		no	Vaccine	murine (IgG2a)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Integrase **References** Bizub-Bender1994 • 16: BALBc mice were immunized with rec integrase, hybridomas expressing anti-integrase Abs were generated, and the antibodies characterized [Bizub-Bender1994]				
228	1C12B1	Pol	RT (431–521)			Vaccine	murine
		Vaccine *Vector/Type:* recombinant protein *HIV component:* RT **References** Ferns1991 • 1C12B1: Recognized both p66 and p51 in Western blot, binds to C terminus [Ferns1991] • 1C12B1: UK Medical Research Council AIDS reagent: ARP384					
229	21	Pol	Integrase (58–141)		no	Vaccine	murine (IgG2b)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Integrase **References** Bizub-Bender1994, Levy-Mintz1996 • 21: BALBc mice were immunized with rec integrase, hybridomas expressing anti-integrase Abs were generated, and the antibodies characterized [Bizub-Bender1994] • 21: Used for the creation of single chain variable antibody fragments (SFvs) for internal cellular expression – neutralization of IN activity prior to integration, whether the Ab is expressed in the nucleolus or the cytoplasm – relative binding affinity to IN: 12 > 17 = 33 > 21 > 4 [Levy-Mintz1996]				
230	32 (mAb32, Fab32)	Pol	Integrase (223–266)		no	Vaccine	murine (IgG2b)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Integrase					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Bizub-Bender1994, Yi2000a, Yi2002					
		• 32: BALBc mice were immunized with rec integrase, hybridomas expressing anti-integrase Abs were generated, and the antibodies characterized – MAbs 32 and 33 form a competition group [Bizub-Bender1994]					
		• 32: Limited proteolysis combined with mass spectrometric analysis indicates Fab32 binds to two strands of the beta sheet, beta1 223F, 224R, 226Y, and 228R and beta5 264K and 266K [Yi2000a]					
		• 32: Called mAb32 – mAb33 and mAb32 compete for binding to the C-term domain of Integrase – while mAb32 only weakly inhibits IN activity, mAb33 inhibits strongly, mAb32 has a lower affinity than mAb33, and Fab32 does not inhibit at all while Fab33 inhibits DNA binding a catalytic activity [Yi2002]					
231	35	Pol	Integrase (1–58)		no	Vaccine	murine (IgG2b)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Integrase					
		References Bizub-Bender1994					
		• 35: There appears to be two IN Abs with similar names: MAb 35 and 35 [Barsov1996, Bizub-Bender1994]					
		• 35: BALBc mice were immunized with rec integrase, hybridomas expressing anti-integrase Abs were generated, and the antibodies characterized – the Zn finger motif is in the binding region – MAbs 12, 13 and 35 form a competition group [Bizub-Bender1994]					
232	3D12	Pol	RT			Vaccine	murine (IgG2a)
		Vaccine *Vector/Type:* vaccinia *HIV component:* RT					
		References Chiba1997					
		• 3D12: There is an anti-Nef MAb that also has this name (see [Chiba1997])					
233	3F10	Pol	RT			Vaccine	murine (IgG2a)
		Vaccine *Vector/Type:* vaccinia *HIV component:* RT					
		References Chiba1997					
234	4	Pol	Integrase (141–172)		no	Vaccine	murine (IgG2b)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Integrase					
		References Bizub-Bender1994, Levy-Mintz1996					
		• 4: There is another MAb with this ID that reacts with gp41 [Oldstone1991, Bizub-Bender1994]					
		• 4: BALBc mice were immunized with rec integrase, hybridomas expressing anti-integrase Abs were generated, and the antibodies characterized – 4 has a low binding affinity [Bizub-Bender1994]					
		• 4: Used for the creation of single chain variable antibody fragments (SFvs) for internal cellular expression – neutralization of IN activity prior to integration, whether the Ab is expressed in the nucleolus or the cytoplasm – relative binding affinity to IN: 12 > 17 = 33 > 21 > 4 [Levy-Mintz1996]					
235	6B9	Pol	RT			Vaccine	murine (IgG2a)
		Vaccine *Vector/Type:* vaccinia *HIV component:* RT					
		References Chiba1997					
236	7C4	Pol	RT			Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* vaccinia *HIV component:* RT					
		References Chiba1997					
		• 7C4: Dose-dependent inhibition of polymerase activity of RT of strains IIIB, Bru and IMS-1, but not HIV-2 strains GH-1 or LAV-2 or SIV strains MAC or MND [Chiba1997]					
237	RT-4	Pol	RT		no		murine (IgG2b)
		References Li1993, Gu1996					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• RT-4: Increased nevirapine and delavirdine inhibition, no effect on AZT inhibition [Gu1996]					
238	RT7O	Pol	RT (231–315)			Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* RT **Donor** B. Ferns and R. Tedder **References** Ferns1991 • RT7O: Conformational epitope located centrally in the protein – inhibited RT enzyme activity and thus may bind close to the active site of the enzyme [Ferns1991] • RT7O: UK Medical Research Council AIDS reagent: ARP381					
239	RT7U	Pol	RT (231–315)			Vaccine	murine
		Vaccine *Vector/Type:* recombinant protein *HIV component:* RT **Donor** B. Ferns and R. Tedder **References** Ferns1991 • RT7U: Has a conformational epitope – reacts with p66 and p51 in WB [Ferns1991] • RT7U: UK Medical Research Council AIDS reagent: ARP380					
240	anti-HIV-1 RT	Pol	RT				murine (IgG)
		References diMarzo Veronese1986, Maciejewski1995, Wainberg1995 • anti-HIV-1 RT: Cloned heavy and light chains to express Fab intracellularly, preventing HIV infection in vitro – this MAb was broadly cross-reactive with clinical strains and even HIV-2 [Maciejewski1995] • Commentary on Maciejewski et al. [Wainberg1995]					
241	polyclonal	Pol	p55		no	Vaccine	Rhesus macaque
		Vaccine *Vector/Type:* virus-like particle *HIV component:* Pr55gag, anchored gp120, V3+CD4 linear domains **References** Wagner1998b • A VLP is a non-infectious virus-like particle self-assembled from HIV Pr55 gag – macaques were immunized with VLPs bound to either gp120 or V3+CD4 linear domains – gag and env CTL specific CTL were stimulated in each case, and Ab response to gag and gp120 and was elicited, but the gp120 neutralizing response occurred only with whole gp120, not V3+CD4 – despite the CTL and Ab response, immunized macaques were infected by intervenous challenge with SHIV chimeric challenge stock [Wagner1998b]					
242	polyclonal	Pol	RT			Vaccine	murine
		Vaccine *Vector/Type:* DNA *HIV component:* Gag, Pol, Vif, Env *Adjuvant:* B7, IL-12 **References** Kim1997b • A gag/pol, vif or CMN160 DNA vaccine, when delivered in conjunction with the plasmid encoding the co-stimulatory molecules B7 and IL-12, gave a dramatic increase in both the cytotoxic and proliferative responses in mice, as well as Ab response detected by ELISA [Kim1997b]					
243	polyclonal	Pol	RT (203–219)			Vaccine	murine (IgA)
		Vaccine *Vector/Type:* Salmonella *HIV component:* RT **References** Burnett2000 • A live attenuated bacterial vaccine, Salmonella SL3261-pHART, with an inserted HIV RT gene fragment in the Lpp-OmpA-HIV fusion protein, induced a lymphoproliferative Th response and fecal RT-specific IgA in BALB/c mice [Burnett2000]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
244	33 (mAb33, Fab33, 33D5, mab 33)	Pol	Integrase (223–268 HXB2)		no	Vaccine	murine (IgG2b)

Vaccine *Vector/Type:* recombinant protein *HIV component:* Integrase
Ab type C-term
References Bizub-Bender1994, Levy-Mintz1996, Yi2000a, Yi2002

- 33: BALBc mice were immunized with rec integrase, hybridomas expressing anti-integrase Abs were generated, and the antibodies characterized – MAbs 32 and 33 form a competition group [Bizub-Bender1994]
- 33: Used for the creation of single chain variable antibody fragments (SFvs) for internal cellular expression – neutralization of IN activity prior to integration, whether the Ab is expressed in the nucleolus or the cytoplasm – relative binding affinity to IN: 12 > 17 = 33 > 21 > 4 [Levy-Mintz1996]
- 33: Limited proteolysis combined with mass spectrometric analysis were used to define the binding site for Fab32, but Fab33 binding to the Intergrase C-term domain left it resistant to proteolytic digestion [Yi2000a]
- 33: Called mAb33 – mAb33 and mAb32 compete for binding to the C-term domain of Integrase – while mAb32 only weakly inhibits IN activity, mAb33 inhibits strongly, mAb32 has a lower affinity than mAb33, and Fab32 does not inhibit at all while Fab33 inhibits catalytic activity and DNA binding – heteronuclear NMR indicated eight residues of Integrase are immobilized upon Fab33 binding, two in the core of the protein, and 6 on the outer face that form a contiguous patch likely to contain the epitope – 223F, 224R, 226Y, 244K, 267I, and 268I, which may be a useful target for drug design – the Fab33-IN complex is far more soluble than IN alone and may be useful for crystallization [Yi2002]

IV-C-10 Vif Antibodies

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
245	TG002	Vif (34–47)	Vif (34–47)	KARGWFYRHHYESP?	no	Vaccine	murine
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Vif **Donor** Transgene • TG002: This MAb was raised in response to a rec Vif protein derived from E. coli • TG002: NIH AIDS Research and Reference Reagent Program: 2746					
246	TG001	Vif (176–192)	Vif (176–192)	KPQKTKGHRGSHTMNGH?	no	Vaccine	murine
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Vif **Ab type** C-term **Donor** Transgene • TG001: This antibody was raised in response to a rec Vif protein derived from E. coli • TG001: NIH AIDS Research and Reference Reagent Program: 2745					
247	J4	Vif	(HXB2)				chimeric rabbit/human FAb
		References Goncalves2002 • J4: The authors developed a Vif-specific intrabody single-chain FAb fragment of J4 called 14BL – when expressed intracellularly in the cytoplasm this intrabody efficiently bound Vif protein and neutralized its infectivity enhancing function – intrabody-expressing transduced cells were shown to be highly refractory to challenge with the laboratory strain NL43 and with primary isolates strains of HIV-1 [Goncalves2002]					
248	polyclonal	Vif	Vif			Vaccine	murine
		Vaccine *Vector/Type:* DNA *HIV component:* Gag, Pol, Vif, Env *Adjuvant:* B7, IL-12 **References** Kim1997b • A gag/pol, vif or CMN160 DNA vaccine, when delivered in conjunction with the plasmid encoding the co-stimulatory molecules B7 and IL-12, gave a dramatic increase in both the cytotoxic and proliferative responses in mice, as well as an Ab response detected by ELISA [Kim1997b]					

IV-C-11 Tat Antibodies

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
249	NT3/2D1.1	Tat (2–15)	Tat	EPVDPNLEPWNHPS		Vaccine	murine (IgG1a)
		Vaccine *Vector/Type:* peptide *HIV component:* Tat **Ab type** N-term **References** Dingwall1989 • NT3/2D1.1: Immunoprecipitates and immunoblots HIV-1 tat protein [Dingwall1989] • NT3/2D1.1: UK Medical Research Council AIDS reagent: ARP352					
250	1.2	Tat (2–17)	Tat (1–16)	EPVDPRLEWKHPGSQ			
		References Ovod1992, Ranki1995 • 1.2: Weak expression of Tat observed in HIV+ brain tissue sample, in contrast to Nef [Ranki1995]					
251	1D9D5	Tat (2–21)	Tat	EPVDPRLEWKHPGSQPKTA		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Tat **Ab type** N-term **References** Mhashilkar1995, Valvatne1996 • 1D9D5: Single chain antibodies, intrabodies, were engineered that can be stably expressed in the cytoplasm of mammalian cells – co-expression of an N-term intrabody can inhibit transactivation of an HIV LTR-CAT construct and block import into nucleus, but intrabody specific for exon 2 did not inhibit activity [Mhashilkar1995] • 1D9D5: Exogenously delivered Tat can efficiently transactivate an HIV-LTR-CAT construct in HeLa cells in the presence of 1D9D5, suggesting when considered with the results of [Mhashilkar1995], that free Tat and not Ab bound is taken up by cells [Valvatne1996]					
252	1D2F11	Tat (49–86)	Tat	RKKRRQRRRPPQGSQTHQVSLSKQP-TSQSRGDPTGPKE		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Tat **Ab type** C-term **References** Valvatne1996 • 1D2F11: MAb did not bind shorter peptides – this MAb inhibited exogenously delivered Tat transactivation of an HIV-LTR-CAT construct in HeLa cells by inhibition of cellular uptake of Tat [Valvatne1996]					
253	2D9E7	Tat (49–86)	Tat	RKKRRQRRRPPQGSQTHQVSLSKQP-TSQSRGDPTGPKE		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Tat **Ab type** C-term **References** Valvatne1996 • 2D9E7: MAb did not bind shorter peptides – this MAb inhibited exogenously delivered Tat transactivation of an HIV-LTR-CAT construct in HeLa cells by inhibition of cellular uptake of Tat, but less efficiently than MAbs 1D2F11 or 4B4C4 [Valvatne1996]					
254	4B4C4 (4B4)	Tat (49–86)	Tat	RKKRRQRRRPPQGSQTHQVSLSKQP-TSQSRGDPTGPKE		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Tat **Ab type** C-term **References** Valvatne1996, Jensen1997					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 4B4C4: MAb did not bind shorter peptides – this MAb inhibited exogenously delivered Tat transactivation of an HIV-LTR-CAT construct in HeLa cells by inhibition of cellular uptake of Tat [Valvatne1996]					
255	5G7D8	Tat (49–86)	Tat	RKKRRQRRRPPQGSQTHQVSLSKQP-TSQSRGDPTGPKE		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Tat **Ab type** C-term **References** Valvatne1996 • 5G7D8: MAb did not bind shorter peptides – this MAb inhibited exogenously delivered Tat transactivation of an HIV-LTR-CAT construct in HeLa cells by inhibition of cellular uptake of Tat, but less efficiently than 1D2F11 or 4B4C4 [Valvatne1996]					
256	NT2/4D5.24	Tat (73–86)	Tat	PTSQPRGDPTGPKE		Vaccine	murine
		Vaccine *Vector/Type:* peptide *HIV component:* Tat **Ab type** C-term **References** Dingwall1989 • NT2/4D5.24: Immunoprecipitates and immunoblots HIV-1 tat protein [Dingwall1989]					
257	L-anti-Tat	Tat	Tat		L P (when lipidated)	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Tat **Donor** AGMED, Inc., Bedford, MA USA **References** Cruikshank1997 • L-anti-Tat: Lipidated antibody can be taken up by cells and effectively block IIIB and primary virus HIV-1 replication in actively and latently infected cells [Cruikshank1997]					
258	2D9D5	Tat	Tat			Vaccine	murine (IgG)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Tat **Ab type** C-term **References** Mhashilkar1995 • 2D9D5: Single chain antibodies, intrabodies, were engineered that can be stably expressed in the cytoplasm of mammalian cells – co-expression of C-term intrabody did not inhibit transactivation of an HIV LTR-CAT construct, in contrast to MAb 1D9D5 [Mhashilkar1995]					

IV-C-12 Rev Antibodies

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
259	4G9	Rev (5–15)	Rev (5–15)	SGDSDEELIRT?		Vaccine	murine
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Rev **References** Jensen1997 • 4G9: Mapped binding location by protein footprinting [Jensen1997]					
260	Ab2	Rev (32–50)	Rev (32–49 BRU)	EGTRQARRNRRRWRERQR		Vaccine	(IgG1)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Rev **Donor** Tony Lowe and Jonathan Karn, MRC Center, Cambridge **References** Henderson1997 • Ab2: The Ab2 binding site overlaps the nuclear localization signal – Ab2 binding to Rev was blocked by bound HIV RNA – the cellular protein importin-beta can bind in this Arg rich region – atypically, the Rev binds specifically to importin-beta, but not to the importin-beta-importin-alpha dimer [Henderson1997]					
261	10.1	Rev (33–48)	Rev (33–48)	GTRQARRNRRRRWRER?			
		References Ovod1992, Ranki1994, Ranki1995, Maksiutov2002 • 10.1: Binds to the RRE binding site – polyclonal anti-Rev Ab detected Rev in astrocytes in 4/5 brain autopsy samples, but only one of these was positive using 10.1, suggesting most Rev was bound to RRE [Ranki1995] • 10.1: This epitope is similar to a fragment of the human protein Complement 4 (containing C4A anaphlylatoxin), GRRNRRRR [Maksiutov2002].					
262	3H6	Rev (38–43)	Rev (38–44)	RRNRRR		Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Rev **References** Orsini1995, Maksiutov2002 • 3H6: There is another MAb with this ID that recognizes gp41 [Pinter1995] • 3H6: Directed against nucleolar localization/RRE binding domain – antigenic domain tentative, MAb failed to bind a RRNRRR Rev deletion mutant [Orsini1995] • 3H6: This epitope is similar to a fragment of the human protein Complement 4 (containing C4A anaphlylatoxin), GRRNRRRR [Maksiutov2002].					
263	8E7	Rev (70–84)	Rev (70–84)	PVPLQLPPLERLTLD		Vaccine	murine (IgG2aκ)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Rev **References** Kalland1994a, Kalland1994b, Szilvay1995, Jensen1997, Boe1998, Maksiutov2002 • 8E7: 8E7 worked in indirect immunofluorescence and also detected Rev in WB assays – used to detect localization of Rev in several compartments including the nucleoli, nucleoplasm, perinuclear zone, and cytoplasm – Rev co-localized with host cell factors known to assemble on nascent transcripts – Rev shuttles continuously between cytoplasmic and nucleoplasmic compartments [Kalland1994a, Kalland1994b, Szilvay1995] • 8E7: Peptide interaction mapped to aa 70-84, 75-88 – protein footprint to 65-88 [Jensen1997] • 8E7: HIV-1 RNA and Rev localize to the same region in the nucleoplasm, but the splicing factor SC-35 localizes in different speckles with the nucleoplasm than Rev – intron containing beta-globin was distributed similarly to HIV-1, suggesting Rev and HIV-1 RNAs interact at putative sites of mRNA transcriptions and splicing [Boe1998] • 8E7: This epitope is similar fragments of the human protein Epidermal growth factor receptor substrate 15, EPVPMSLPPA, and Insulin-like growth factor binding protein complex acid labile chain precursor, QPPGLERLWLEGNPWDCG [Maksiutov2002]					
264	9G2 (9G2G4D6E8)	Rev (70–84)	Rev (70–84)	PVPLQLPPLERLTLD		Vaccine	murine (IgG2aκ)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Rev					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		Donor Anne Marie Szilvay **References** Kalland1994a, Jensen1997, Maksiutov2002 • 9G2: Worked in indirect immunofluorescence and also detected Rev in WB assays – used to detect localization of Rev throughout the cell [Kalland1994a] • 9G2: Peptide interaction mapped to aa 70-84, 75-88 – protein footprint to 65-88 [Jensen1997] • 9G2: This epitope is similar fragments of the human protein Epidermal growth factor receptor substrate 15, EPVPMSLPPA, and Insulin-like growth factor binding protein complex acid labile chain precursor, QPPGLERLWLEGNPWDCG [Maksiutov2002] • 9G2: Called 9G2G4D6E8: UK Medical Research Council AIDS reagent: ARP3058					
265	Ab4	Rev (72–91)	Rev (72–91 BRU)	PLQLPPLERLTLDCNEDCGT		Vaccine	(IgG1)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Rev **Donor** Tony Lowe and Jonathan Karn, MRC Center, Cambridge **References** Henderson1997, Maksiutov2002 • Ab4: The binding site overlaps the nuclear export signal – binding was not blocked by bound HIV RNA and may be accessible for protein interaction [Henderson1997] • Ab4: This epitope is similar fragments of the human protein Epidermal growth factor receptor substrate 15, EPVPMSLPPA, and Insulin-like growth factor binding protein complex acid labile chain precursor, QPPGLERLWLEGNPWDCG [Maksiutov2002]					
266	3G4	Rev (90–116)	Rev (90–116)	GTSGTQGVGSPQILVESPTVLESGT-KE?		Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Rev **References** Orsini1995 • 3G4: Binds to a region that can be dispensed with and still retain Rev function [Orsini1995]					
267	1G10 (IG10F4)	Rev (96–105)	Rev (95–105)	GVGSPQILVE		Vaccine	murine (IgG2bκ)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Rev **Donor** Anne Marie Szilvay **References** Kalland1994a • 1G10: Bound Rev in indirect immunofluorescence and also detected Rev in WB – used to detect localization of Rev throughout the cell [Kalland1994a] • 1G10: Peptide interaction mapped to aa 91-105, 96-110 – protein footprint to aa 10-20, and 95-105 [Jensen1997] • 1G10: Called IG10F4: UK Medical Research Council AIDS reagent: ARP3060					
268	1G7	Rev (96–105)	Rev (95–105)	GVGSPQILVE		Vaccine	murine (IgG2bκ)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Rev **References** Kalland1994a, Jensen1997 • 1G7: Worked in indirect immunofluorescence and also detected Rev in WB – used to detect localization of Rev throughout the cell [Kalland1994a] • 1G7: Peptide interaction mapped to aa 91-105, 96-110 – protein footprint to aa 95-105 [Jensen1997]					
269	Ab3	Rev (102–116)	Rev (102–116 BRU)	ILVESPTVLESDKTE		Vaccine	(IgG1)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Rev **Donor** Tony Lowe and Jonathan Karn, MRC, Cambridge **References** Henderson1997 • Ab3: This binding site is at the carboxy end of Rev – Ab3 binding was not blocked by bound HIV RNA [Henderson1997]					
270	2G2	Rev	Rev			Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Rev					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

References Orsini1995

- 2G2: Does not bind to any of a set of glutathione S-transferase (GST) Rev fusion proteins, or to Rev in a RIPA buffer, suggesting a conformational epitope [Orsini1995]

IV-C-13 gp160 Antibodies

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
271	M85	gp160 (30–51)	gp120 (30–51 LAI)	ATEKLWVTVYYGVPVWKEATTT	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* Env **Ab type** C1 **Donor** Fulvia di Marzo Veronese **References** diMarzo Veronese1992, Moore1994c, Moore1994d, Moore1996, Ditzel1997, Wyatt1997 • M85: Immunoblot and RIP reactive for strains IIIB, 451, MN, RF, and RUTZ – binds deglycosylated gp120 [diMarzo Veronese1992] • M85: C1 domain – mutation 40 Y/D impairs binding – the relative affinity for denatured/native gp120 is < .01, suggesting conformational component [Moore1994c] • M85: Binding inhibited by MAb 4D4#85, enhanced by conformationally sensitive anti-V3 MAb 5G11, and some anti-18 MAbs [Moore1996] • M85: Binds efficiently to sgp120 but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding [Wyatt1997]			
272	7E2/4	gp160 (31–50)	gp120 (31–50 LAI)	TEKLWVTVYYGVPVWKEATT		Vaccine	murine (IgG)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Env **Ab type** C1 **Donor** S. Ranjbar, NIBSC, UK **References** Moore1994c, Maksiutov2002 • 7E2/4: C1 domain – the relative affinity for denatured/native gp120 is .07, suggesting conformational component [Moore1994c] • 7E2/4: This epitope has a high degree of similarity with the platelet membrane glycoprotein IIIA precursor (GLIIIA) (integrin beta- 3) (CD61): PLYKEATSTF [Maksiutov2002] • 7E2/4: UK Medical Research Council AIDS reagent: ARP3050			
273	4D4#85	gp160 (41–50)	gp120 (LAI)	GVPVWKEATT		Vaccine	murine (IgG)
		Vaccine *Strain:* LAI *HIV component:* Env **Ab type** C1 **Donor** S. Nigida and L. Arthur, NCI, Frederick, MD USA **References** Moore1994c, Moore1994d, Moore1996, Wyatt1997, Binley1998, Maksiutov2002 • 4D4#85: C1 domain – the relative affinity, denatured/native gp120 is 0.1 – mutation 45 W/S impairs binding [Moore1994c] • 4D4#85: Inhibits binding of C1 MAb M85, C1-C5 discontinuous epitope MAbs 181 and 212A, and CD4 binding induced MAbs 48d and 17b [Moore1996] • 4D4#85: Binds efficiently to sgp120 but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding – does not bind to HXBc2 gp120 if the 19 C-term amino acids, in conjunction with C1 positions 31-50, are deleted [Wyatt1997] • 4D4#85: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer [Binley1998] • 4D4#85: This epitope has a high degree of similarity with the platelet membrane glycoprotein IIIA precursor (GLIIIA) (integrin beta- 3) (CD61): PLYKEATSTF [Maksiutov2002]			
274	M92	gp160 (41–50)	gp120 (31–50 LAI)	GVPVWKEATT	no	Vaccine	rat (IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* Env **Ab type** C1 **Donor** Fulvia di Marzo Veronese **References** diMarzo Veronese1992, Moore1994c, Moore1994d, Maksiutov2002 • M92: Immunoblot reactive, RIP negative, but precipitates deglycosylated gp120 – reacts with strains IIIB, 451, MN, RF, and RUTZ [diMarzo Veronese1992] • M92: The relative affinity for denatured/native gp120 is 1 [Moore1994c]			

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• M92: This epitope has a high degree of similarity with the platelet membrane glycoprotein IIIA precursor (GLIIIA) (integrin beta- 3) (CD61): PLYKEATSTF [Maksiutov2002]					
275	M86	gp160 (42–61)	gp120 (42–61 LAI)	VPVWKEATTTLFCASDAKAY	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* Env **Ab type** C1 **Donor** Fulvia di Marzo Veronese **References** diMarzo Veronese1992, Moore1994c, Maksiutov2002 • M86: Immunoblot and RIP reactive for strains IIIB, 451, MN, RF, and RUTZ – binds deglycosylated gp120 [diMarzo Veronese1992] • M86: C1 domain – the relative affinity for denatured/native gp120 is 1 [Moore1994c] • M86: This epitope has a high degree of similarity with the platelet membrane glycoprotein IIIA precursor (GLIIIA) (integrin beta- 3) (CD61): PLYKEATSTF [Maksiutov2002]					
276	polyclonal	gp160 (52–71)	Env (42–61 LAI)	LFCASDAKAYDTEVHNVWAT	no	Vaccine	murine
		Vaccine *Vector/Type:* vaccinia *HIV component:* Env **Ab type** C1 **References** Collado2000 • Vaccinia p14 can elicit NAbs and p39 tends to be immunodominant, so these two proteins were fused to regions of HIV-1 Env – reduced glycosylation was noted when p14 or p39 was placed in the N-term region of the fusion protein – chimeric proteins shifted the Env Ab response from V3 to either a C1 or C4 domain, depending on the construct – all chimeric Env proteins: 14kEnv, 39kEnv, and Env39k elicited a strong Ab response to the C1 region of gp120 (LFCASDAKAYDTEVHNVWAT), and Env39k mounted a strong response to the C4 region (KAMYAPPISGQIRCSSNITG) [Collado2000]					
277	133/237	gp160 (61–70)	gp120 (51–70 LAI)	YDTEVHNVWA	L	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* IIIB *HIV component:* gp120 **Ab type** C1 **References** Niedrig1992b, Moore1994c, Moore1994d • 133/237: Region of overlap for reactive peptides is WATHA – weak neutralization of lab strains [Niedrig1992b] • 133/237: The relative affinity, denatured/native gp120 is 1.4 – mutation of position 69 W/L impairs binding [Moore1994c]					
278	133/290	gp160 (61–70)	gp120 (61–70 LAI)	YDTEVHNVWA	L	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* IIIB *HIV component:* gp120 **Ab type** C1 **References** Niedrig1992b, Thali1993, Moore1994c, Moore1994d, Wyatt1995, Binley1997a, Wyatt1997, Binley1998 • 133/290: Region of overlap for reactive peptides is WATHA – weak neutralization of lab strains [Niedrig1992b] • 133/290: The relative affinity for denatured/native gp120 is 2.2 – mutation in position 69 W/L impairs binding [Moore1994c] • 133/290: Used for antigen capture assay, either to bind gp120 to the ELISA plate, or to quantify bound gp120 [Wyatt1995] • 133/290: Reciprocal binding inhibition with the antibody 522-149, that binds to a discontinuous epitope – binding is enhanced by some C5 and C1 binding site antibodies [Moore1996] • 133/290: Binds efficiently to sgp120 but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding [Wyatt1997] • 133/290: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer [Binley1998]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 133/290: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) that preserve and expose some neutralizing epitopes while occluding some non-neutralizing epitopes – CD4BS MAbs (F105 and F91) and CD4i (17b and 48d) recognized gp140-GNC4 as well as gp120 or gp140 – non-neutralizing MAbs C11, A32, 522-149, M90, and #45 bound to the gp140-GNC4 glycoprotein at reduced levels compared to gp120 – MAbs directed at the extreme termini of gp120 C1 (135/9 and 133/290) and C5 (CRA-1 and M91) bound efficiently to gp140-GNC4 [Yang2000]					
279	133/11	gp160 (64–78)	gp120 (64–78)	EVHNVWATHACVPTD	L	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* IIIB *HIV component:* gp120 **Ab type** C1 **References** Niedrig1992b • 133/11: Region of overlap for reactive peptides is WATHA – weak neutralization of lab strains [Niedrig1992b]					
280	D/3G5	gp160 (73–82)	gp120 (73–82 LAI)	ACVPTDPNPQ	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* gp120 **Ab type** C1 **References** Bristow1994 • D/3G5: C1 MAb generated in a study of the humoral immune response to Baculovirus-expressed mis-folded rgp120 and rgp160 [Bristow1994]					
281	D/6A11	gp160 (73–82)	gp120 (73–82 LAI)	ACVPTDPNPQ	no	Vaccine	murine
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* gp120 **Ab type** C1 **References** Bristow1994 • D/6A11: C1 MAb generated in a study of the humoral immune response to Baculovirus-expressed mis-folded rgp120 and rgp160 [Bristow1994]					
282	D/5E12	gp160 (73–92)	gp120 (73–92 LAI)	ACVPTDPNPQEVVLVNVTEN	no	Vaccine	murine
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* gp120 **Ab type** C1 **References** Bristow1994 • D/5E12: C1 MAb generated in a study of the humoral immune response to Baculovirus-expressed mis-folded rgp120 and rgp160 [Bristow1994]					
283	L5.1	gp160 (79–93)	gp120 (89–103 IIIB)	PNPQEVVLVNVTENF		Vaccine	murine (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* gp160 **Ab type** C1 **References** Akerblom1990					
284	4A7C6	gp160 (81–90)	gp120 (81–90 LAI)	PQEVVLVNVT		Vaccine	murine (IgG)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Env **Ab type** C1 **Donor** R. Tedder **References** Thiriart1989, Thali1993, Moore1993a, Moore1994c, Moore1994d, Moore1996 • 4A7C6: Bound preferentially to denatured IIIB gp120 [Moore1993a] • 4A7C6: The relative affinity for denatured/native gp120 is 7.9 – mutation 88 N/P impairs binding [Moore1994c] • 4A7C6: C1 region epitope (88 N/P substitutions abrogates binding), but substitutions 380 G/F and 420 I/R also impaired binding [Moore1994d] • 4A7C6: Reciprocal binding inhibition with the antibody 133/192 – enhanced by anti-C5 antibodies, and C1 antibody 135/9 [Moore1996] • 4A7C6: UK Medical Research Council AIDS reagent: ARP 360					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
285	1D10	gp160 (81–100)	gp120 (81–100 LAI)	PQEVVLVNVTENFDMWKNDM	L	Vaccine	rat
		Vaccine *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* gp120 **Ab type** C1 **References** Dowbenko1988, Berman1991, Nakamura1992, Moore1994c • 1D10: Cross-blocks 5B3 in IIIB-rsgp160 ELISA – type specific in rgp120 ELISA binding [Nakamura1992] • 1D10: The relative affinity for denatured/native gp120 is 13 – mutation 88 N/P impairs binding [Moore1994c]					
286	B242	gp160 (83–92)	gp120 (83–92 LAI)	EVVLVNVTEN	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *Strain:* NL43 *HIV component:* gp160 **Ab type** C1 **References** Bristow1994 • B242: C1 MAb generated in a study of the humoral immune response to Baculovirus-expressed mis-folded rgp160 IIIB:NL43, MicroGenSys [Bristow1994]					
287	133/192	gp160 (91–100)	gp120 (91–100 LAI)	ENFDMWKNDM	L	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* IIIB *HIV component:* gp120 **Ab type** C1 **Donor** Matthias Niedrig **References** Niedrig1992b, Moore1993c, Moore1994c, Moore1996, Trkola1996a, Binley1997a, Binley1998 • 133/192: Epitope seems complex, binds multiple peptides – weak neutralization of lab strain [Niedrig1992b] • 133/192: The relative affinity for denatured/native gp120 is 1.8 [Moore1994c] • 133/192: C1 region – substitutions 76P/Y, 113 D/A or R, 117 K/W, 420 I/R, 427 W/S impair binding, other substitutions enhanced binding [Moore1994d] • 133/192: Reciprocal binding inhibition with the antibody 4A7C6 – enhanced by some anti-C5 and-C1 antibodies [Moore1996] • 133/192: Does not neutralize JR-FL nor block gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study [Trkola1996a] • 133/192: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer [Binley1998]					
288	489.1(961)	gp160 (91–100)	gp120 (91–100 LAI)	ENFDMWKNDM		Vaccine	murine (IgG)
		Vaccine *Strain:* LAI *HIV component:* Env **Ab type** C1 **Donor** C. Bruck, SKB, Belgium **References** Moore1994c • 489.1(961): The relative affinity for denatured/native gp120 is 1 [Moore1994c] • 489.1(961): NIH AIDS Research and Reference Reagent Program: 961					
289	5B3	gp160 (91–100)	gp120 (91–100 LAI)	ENFDMWKNDM	no	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* gp160 **Ab type** C1 **References** Berman1991, Nakamura1992, Beretta1994, Moore1994c • 5B3: Blocks gp120 -CD4 binding [Berman1991] • 5B3: Cross-blocks 1D10 in competitive IIIB-rsgp160 ELISA – no neutralization – blocks IIIB-gp120 sCD4 binding – localized binding to residues 72-106 [Nakamura1992] • 5B3: The relative affinity of denatured/native gp120 is 8.3 [Moore1994c]					
290	B10	gp160 (91–100)	gp120 (91–100 LAI)	ENFDMWKNDM		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* gp160 **Ab type** C1					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Abacioglu1994, Moore1994c • B10: C1 region – epitope boundaries mapped by peptide scanning, FNMW core [Abacioglu1994] • B10: The relative affinity for denatured/native gp120 is 0.4 [Moore1994c] • B10: There is FNM/FDM polymorphism in LAI-based peptides, and N is essential (J. P. Moore, per. comm.)					
291	B2	gp160 (91–100)	gp120 (91–100 LAI)	ENFDMWKNDM		Vaccine	murine (IgG2b)
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* gp160 **Ab type** C1 **References** Thali1993, Abacioglu1994, Moore1994c, Moore1994d, Binley1997a • B2: C1 region – epitope boundaries mapped by peptide scanning, FNMW core [Abacioglu1994] • B2: The relative affinity for denatured/native gp120 is 1.4 [Moore1994c] • B2: There is FNM/FDM polymorphism in LAI-based peptides, and N is essential (J. P. Moore, per. comm.)					
292	C6 (Ch6)	gp160 (91–100)	gp120 (91–100 LAI)	ENFDMWKNDM		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* gp160 **Ab type** C1 **References** Pincus1993a, Abacioglu1994, Moore1994c, Pincus1996 • C6: C1 region – epitope boundaries mapped by peptide scanning, FNMW core [Abacioglu1994] • C6: The relative affinity for denatured/native gp120 is 0.9 [Moore1994c] • C6: There is FNM/FDM polymorphism in LAI-based peptides – N is essential (J. P. Moore, per. comm.) • C6: Called Ch6 – binds to gp120 but not to infected cells – when linked to ricin A, the immunotoxin did not mediate cell killing – sCD4 has no effect [Pincus1993a, Pincus1996] • C6: NIH AIDS Research and Reference Reagent Program: 810					
293	MF49.1	gp160 (91–100)	gp120 (91–100 LAI)	ENFDMWKNDM		Vaccine	murine (IgG)
		Vaccine *Strain:* LAI *HIV component:* Env **Ab type** C1 **References** Thiriart1989, Moore1994c • MF49.1: The relative affinity of denatured/native gp120 is 3.8 [Moore1994c]					
294	T1.1	gp160 (91–100)	gp120 (91–100 LAI)	ENFDMWKNDM		Vaccine	murine (IgG)
		Vaccine *Vector/Type:* vaccinia *HIV component:* gp160 **Ab type** C1 **References** Akerblom1990, Broliden1990, Moore1994c • T1.1: Also reacted in solid phase with gp120(234-248) NGTGPCTNVSTQCT [Akerblom1990] • T1.1: No ADCC activity – reactive peptide: NVTENFNMWKNDMVEQ, IIIB [Broliden1990] • T1.1: C1 region – the relative affinity for denatured/native gp120 is 1 [Moore1994c]					
295	T7.1	gp160 (91–100)	gp120 (91–100 LAI)	ENFDMWKNDM		Vaccine	murine (IgG)
		Vaccine *Strain:* LAI *HIV component:* Env **Ab type** C1 **References** Akerblom1990, Bolmstedt1990, Moore1994c, Moore1994d • T7.1: The relative affinity of denatured/native gp120 is 4.0 [Moore1994c]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
296	T9	gp160 (91–100)	gp120 (91–100 LAI)	ENFDMWKNDM		Vaccine	murine (IgG)
		Vaccine *Strain:* LAI *HIV component:* Env **Ab type** C1 **Donor** Lennart Akerblom, Britta Wahren and Jorma Hinkula **References** Akerblom1990, Bolmstedt1990, Moore1994c, Moore1994d, Binley1997a • T9: There are two HIV-Abs with the name T9, one binds to gp41, one to gp120 • T9: The relative affinity of denatured/native gp120 is 7.9 [Moore1994c] • T9: Binds to the C1 region – 45 W/S, 88 N/P, 256 S/Y, 262 N/T, 475 M/S, 485 1.83, and 491 I/F enhanced binding, no substitution tested significantly inhibited [Moore1994d]				
297	GV4D3	gp160 (92–100)	gp120 (92–100 IIIB)	NFNMWKNDM		Vaccine	murine
		Vaccine *Vector/Type:* protein-Ab complex *HIV component:* gp120 complexed with MAb M77 **Ab type** C1 **Donor** Patricia Earl and Christopher Broder, NIH **References** Denisova1996 • GV4D3: When anti-V3 MAb M77 was bound to gp120 and used as an immunogen, it stimulated many MAbs to linear epitopes – MAbs GV4H4 and GV5F9 are homologous to GV4D3 and were generated in the same experiment [Denisova1996]				
298	B27	gp160 (93–96)	gp120 (94–97 BH10)	FNMW	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *Strain:* NL43 *HIV component:* gp160 **Ab type** C1 **References** Abacioglu1994, Bristow1994 • B27: C1 region – epitope boundaries mapped by peptide scanning [Abacioglu1994] • B27: C1 MAb generated in a study of the humoral immune response to Baculovirus-expressed mis-folded rgp160 IIIB:NL43, MicroGenSys [Bristow1994]				
299	B9	gp160 (93–96)	gp120 (93–96 LAI)	FNMW		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* gp160 **Ab type** C1 **References** Abacioglu1994 • B9: Binds C1 region – epitope boundaries mapped by peptide scanning [Abacioglu1994]				
300	B35	gp160 (93–98)	gp120 (94–99 BH10)	FNMWKN		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* gp160 **Ab type** C1 **References** Abacioglu1994 • B35: C1 region – epitope boundaries mapped by peptide scanning [Abacioglu1994]				
301	D/4B5	gp160 (93–101)	gp120 (93–101 LAI)	FNMWKNDMV	no	Vaccine	murine
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* gp120 **Ab type** C1 **References** Bristow1994 • D/4B5: C1 MAb generated in a study of the humoral immune response to Baculovirus-expressed mis-folded rgp120 and rgp160 [Bristow1994]				
302	D/5A11	gp160 (93–101)	gp120 (93–101 LAI)	FNMWKNDMV	no	Vaccine	murine
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* gp120 **Ab type** C1					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Bristow1994					
		• D/5A11: C1 MAb generated in a study of the humoral immune response to Baculovirus-expressed mis-folded rgp120 and rgp160 [Bristow1994]					
303	D/6B2	gp160 (93–101)	gp120 (93–101 LAI)	FNMWKNDMV	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* gp120					
		Ab type C1					
		References Bristow1994					
		• D/6B2: C1 MAb generated in a study of the humoral immune response to Baculovirus-expressed mis-folded rgp120 and rgp160 [Bristow1994]					
304	B18	gp160 (101–110)	gp120 (101–110 LAI)	VEQMHEDIIS		Vaccine	murine (IgG2a)
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* gp160					
		Ab type C1					
		References Abacioglu1994, Moore1994c					
		• B18: C1 region – epitope boundaries mapped by peptide scanning, HEDII core [Abacioglu1994]					
		• B18: The relative affinity for denatured/native gp120 is 1 [Moore1994c]					
305	B20	gp160 (101–110)	gp120 (101–110 LAI)	VEQMHEDIIS		Vaccine	murine (IgG2a)
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* gp160					
		Ab type C1					
		References Abacioglu1994, Moore1994c					
		• B20: C1 region – epitope boundaries mapped by peptide scanning – HEDII core [Abacioglu1994]					
		• B20: The relative affinity for denatured/native gp120 is 1 [Moore1994c]					
306	MF39.1 (39.1)	gp160 (101–110)	gp120 (101–110 LAI)	VEQMHEDIIS		Vaccine	murine (IgG)
		Vaccine *Strain:* LAI *HIV component:* Env					
		Ab type C1					
		References Thiriart1989, Cook1994, Moore1994c					
		• MF39.1: Called 39.1, and is probably the same as MF39.1 – MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – MAbs against the N-terminal half of gp120 do not inhibit gp120 binding to GalCer – binding of GalCer to gp120 does not inhibit MAb binding [Cook1994]					
		• MF39.1: The relative affinity of denatured/native gp120 is 30 [Moore1994c]					
307	187.2.1 (187.1)	gp160 (101–120)	gp120 (101–120 LAI)	VEQMHEDIISLWDQSLKPCV		Vaccine	murine (IgG)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Env					
		Ab type C1 **Donor** Claudine Bruck and Clothilde Thiriart					
		References Thiriart1989, Moore1993a, Cook1994, Moore1994c, Moore1994d					
		• 187.2.1: Called 187.1, and is probably the same as 187.2.1 – bound preferentially to denatured IIIB gp120 [Moore1993a]					
		• 187.2.1: Called 187.1, and is probably the same as 187.2.1 – MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – MAbs against the N-terminal half of gp120 do not inhibit gp120 binding to GalCer – binding of GalCer to gp120 does not inhibit MAb binding [Cook1994]					
		• 187.2.1: The relative affinity for denatured/native gp120 is 7 – mutations 113 D/A (not D/R) and 117 K/W impair binding [Moore1994c]					
		• 187.2.1: UK Medical Research Council AIDS reagent: ARP332					
308	37.1.1(ARP 327) (37.1)	gp160 (101–120)	gp120 (101–120 LAI)	VEQMHEDIISLWDQSLKPCV		Vaccine	murine (IgG)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Env					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		Ab type C1 **Donor** Claudine Bruck **References** Thiriart1989, Moore1993a, Moore1994c • 37.1.1: Called 37.1 – bound preferentially to denatured IIIB gp120 [Moore1993a] • 37.1.1: The relative affinity for denatured/native gp120 is 8.6 – mutations 113 D/R (not D/A) and 117 K/W impair binding [Moore1994c] • 37.1.1: UK Medical Research Council AIDS reagent: ARP327					
309	6D8	gp160 (101–120)	gp120 (101–120 LAI)	VEQMHEDIISLWDQSLKPCV		Vaccine	rat
		Vaccine *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* gp120 **Ab type** C1 **References** Dowbenko1988, Nakamura1992, Moore1994c • 6D8: Highly cross reactive with multiple stains by rgp120 ELISA [Nakamura1992] • 6D8: The relative affinity for denatured/native gp120 is 15 – mutations 113 D/R and 113 D/A impair binding [Moore1994c]					
310	M96	gp160 (101–120)	gp120 (101–120 LAI)	VEQMHEDIISLWDQSLKPCV	no	Vaccine	rat (IgG2a)
		Vaccine *Vector/Type:* protein *HIV component:* Env **Ab type** C1 **Donor** Fulvia di Marzo Veronese **References** diMarzo Veronese1992, Moore1994c, Moore1994d • M96: Immunoblot reactive for strains IIIB, 451, MN, RF, and RUTZ [diMarzo Veronese1992] • M96: C1 region – the relative affinity for denatured/native gp120 is 6 [Moore1994c]					
311	MF119.1	gp160 (101–120)	gp120 (101–120 LAI)	VEQMHEDIISLWDQSLKPCV		Vaccine	murine (IgG)
		Vaccine *Strain:* LAI *HIV component:* Env **Ab type** C1 **References** Thiriart1989, Moore1994c • MF119.1: The relative affinity for denatured/native gp120 is 30 – mutations 113 D/A, 113 D/R, and 117 K/W impair binding [Moore1994c]					
312	MF4.1	gp160 (101–120)	gp120 (101–120 LAI)	VEQMHEDIISLWDQSLKPCV		Vaccine	murine (IgG)
		Vaccine *Strain:* LAI *HIV component:* Env **Ab type** C1 **References** Thiriart1989, Moore1994c • MF4.1: The relative affinity for denatured/native gp120 is 8 [Moore1994c]					
313	MF53.1	gp160 (101–120)	gp120 (101–120 LAI)	VEQMHEDIISLWDQSLKPCV		Vaccine	murine (IgG)
		Vaccine *Strain:* LAI *HIV component:* Env **Ab type** C1 **References** Thiriart1989, Moore1994c • MF53.1: The relative affinity for denatured/native gp120 is 10 [Moore1994c]					
314	MF58.1	gp160 (101–120)	gp120 (101–120 LAI)	VEQMHEDIISLWDQSLKPCV		Vaccine	murine (IgG)
		Vaccine *Strain:* LAI *HIV component:* Env **Ab type** C1 **References** Thiriart1989, Moore1994c					
315	MF77.1	gp160 (101–120)	gp120 (101–120 LAI)	VEQMHEDIISLWDQSLKPCV		Vaccine	murine (IgG)
		Vaccine *Strain:* LAI *HIV component:* Env					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		Ab type C1 **References** Thiriart1989, Moore1994c • MF77.1: The relative affinity for denatured/native gp120 is 11 [Moore1994c]					
316	T2.1	gp160 (101–120)	gp120 (101–120 LAI)	VEQMHEDIISLWDQSLKPCV		Vaccine	murine (IgG)
		Vaccine *Strain:* LAI *HIV component:* Env **Ab type** C1 **Donor** Lennart Akerblom, Britta Wahren and Jorma Hinkula **References** Akerblom1990, Bolmstedt1990, Moore1994c, Moore1994d • T2.1: The relative affinity for denatured/native gp120 is .27 – mutations 113 D/R, 106 E/A, and 117 D/A impair binding [Moore1994c]					
317	11/65 (11/65a/5h)	gp160 (102–121)	gp120 (311–321 HXB10)	EQMHEDIISLWDQSLKPCVK		Vaccine	rat (IgG2b)
		Vaccine *Vector/Type:* recombinant protein *Strain:* BH10 *HIV component:* gp120 **Ab type** C1 **References** McKeating1992a, McKeating1993b, Peet1998 • 11/65: Binds only soluble gp120, not virion bound – used to quantify gp120 shedding – (numbering is incorrect in original?) [McKeating1992a] • 11/65: Called 11/65a/5h – The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind – 11/65 was not affected by V3 serine substitutions – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions [Peet1998] • 11/65: UK Medical Research Council AIDS reagent: ARP3076					
318	W1	gp160 (102–121)	gp120 (102–121 LAI)	EQMHEDIISLWDQSLKPCVK		Vaccine	murine (IgG)
		Vaccine *Strain:* LAI *HIV component:* Env **Ab type** C1 **Donor** D. Weiner, U. Penn. **References** Moore1994c • W1: The relative affinity for denatured/native gp120 is 6 – mutations 113 D/A, 113 D/R, and 117 K/W impair binding [Moore1994c]					
319	T11	gp160 (102–125)	gp120 (102–125)	EQMHEDIISLWDQSLKPCVKLTPL		Vaccine	murine
		Vaccine *Vector/Type:* recombinant protein *HIV component:* oligomeric gp140 **Ab type** C1 **Donor** R. Doms, Univ. of Pennsylvania **References** Earl1994, Jagodzinski1996 • T11: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response [Earl1994] • T11: The sulfated polysaccharide, curdlan sulfate (CRDS), binds to the Envelope of T-tropic viruses and neutralizes virus – deletion of the V3 loop from gp120 results in more potent T11 inhibition by CRDS [Jagodzinski1996]					
320	GV1A8	gp160 (105–113)	gp120 (105–113 IIIB)	HEDIISLWD		Vaccine	murine
		Vaccine *Vector/Type:* protein-Ab complex *HIV component:* gp120 complexed with MAb M77 **Ab type** C1 **References** Denisova1996 • GV1A8: When anti-V3 MAb M77 was bound to gp120 and used as an immunogen, it stimulated many MAbs to linear epitopes – MAbs GV7A4 and GV5H5 are homologous to GV1A8 and were generated in the same experiment [Denisova1996]					
321	11	gp160 (111–120)	gp120 (101–120 LAI)	LWDQSLKPCV		Vaccine	murine (IgG)
		Vaccine *Strain:* LAI *HIV component:* Env **Ab type** C1					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Thiriart1989, Moore1994c • 11: The relative affinity for denatured/native gp120 is 7.8 – mutation 113 D/R impairs binding [Moore1994c]					
322	12G10	gp160 (111–120)	gp120 (101–120 LAI)	LWDQSLKPCV		Vaccine	murine (IgG)
		Vaccine *Strain:* LAI *HIV component:* Env **Ab type** C1 **References** Thiriart1989, Moore1994c • 12G10: The relative affinity for denatured/native gp120 is 17 – mutation 117 K/W impairs binding [Moore1994c]					
323	135/9 (87-135/9)	gp160 (111–120)	gp120 (111–120 LAI)	LWDQSLKPCV	L	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* IIIB *HIV component:* gp120 **Ab type** C1 **Donor** Matthias Niedrig **References** Niedrig1992b, Moore1994c, Moore1994d, Moore1996, Trkola1996a, Binley1997a, Kropelin1998, Yang2000 • 135/9: Defines the epitope as gp120(114-123) MHEDIISLWD (core LWD?) – weak neutralization of lab strain [Niedrig1992b] • 135/9: The relative affinity for denatured/native gp120 is 15 – mutation 113 D/R impairs binding to native and denatured, 113 D/A only to denatured [Moore1994c] • 135/9: Substitutions 106 E/A, 113 D/A or R, and 117 K/W impair binding, some substitutions enhance binding [Moore1994d] • 135/9: Binding is enhanced by some anti-C1 and anti-C5 antibodies – enhances binding of some anti-V3, anti-C4 and anti-V2 MAbs – 135/9 binds to predicted alpha-helix in C1 [Moore1996] • 135/9: Does not neutralize JR-FL nor block gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study [Trkola1996a] • 135/9: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer [Binley1998] • 135/9: Noted to bind to C1 peptide HEDIISLWDQSLK – blocks gp120 interaction with CD4+ cells – blocking activity is additive when combined with antibodies which bind in the C4 region of gp120 (F105, 388/389, and b12) [Kropelin1998] • 135/9: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) that preserve and expose some neutralizing epitopes while occluding some non-neutralizing epitopes – CD4BS MAbs (F105 and F91) and CD4i (17b and 48d) recognized gp140-GNC4 as well as gp120 or gp140 – non-neutralizing MAbs C11, A32, 522-149, M90, and #45 bound to the gp140-GNC4 glycoprotein at reduced levels compared to gp120 – MAbs directed at the extreme termini of gp120 C1 (135/9 and 133/290) and C5 (CRA-1 and M91) bound efficiently to gp140-GNC4 [Yang2000]			
324	7C10	gp160 (111–120)	gp120 (101–120 LAI)	LWDQSLKPCV		Vaccine	murine (IgG)
		Vaccine *Strain:* LAI *HIV component:* Env **Ab type** C1 **References** Thiriart1989, Moore1994c • 7C10: The relative affinity for denatured/native gp120 is 5.8 – mutation 117 K/W impairs binding [Moore1994c]					
325	C4	gp160 (111–120)	gp120 (101–120 LAI)	LWDQSLKPCV		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* gp160 **Ab type** C1 **Donor** George Lewis **References** Abacioglu1994, Moore1993a, Moore1994c • C4: Bound preferentially to denatured IIIB gp120 [Moore1993a] • C4: C1 region – epitope boundaries mapped by peptide scanning, BH10 core IISLW [Abacioglu1994] • C4: The relative affinity for denatured/native gp120 is 10 [Moore1994c]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
326	MF46.1	gp160 (111–120)	gp120 (101–120 LAI)	LWDQSLKPCV		Vaccine	murine (IgG)
		Vaccine *Strain:* LAI *HIV component:* Env **Ab type** C1 **References** Thiriart1989, Moore1994c • MF46.1: The relative affinity for denatured/native gp120 is 8.5 [Moore1994c]					
327	6D5	gp160 (122–141)	gp120 (122–141 LAI)	LTPLCVSLKCTDLKNDTNTN		Vaccine	murine (IgG)
		Vaccine *Strain:* LAI *HIV component:* Env **Ab type** V2 **Donor** S. Nigida and L. Arthur, NCI, Frederick, MD USA **References** Moore1994c, Moore1994d • 6D5: The relative affinity for denatured/native gp120 is 15 – mutations Delta119-205 and 125 L/G impair binding [Moore1994c]					
328	B33	gp160 (123–142)	gp120 (123–142 LAI)	TPLCVSLKCTDLGNATNTNS	no	Vaccine	murine (IgG2bκ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* NL43 *HIV component:* gp160 **Ab type** V2 **Donor** Daniels **References** Abacioglu1994, Bristow1994 • B33: There are two MAbs in the literature named B33, see also gp160(727-734) [Abacioglu1994] • B33: Epitope boundaries mapped by peptide scanning [Abacioglu1994] • B27: C1 MAb generated in a study of the humoral immune response to Baculovirus-expressed mis-folded rgp160 IIIB:NL43, MicroGenSys [Bristow1994] • B33: UK Medical Research Council AIDS reagent: ARP304, gp160/41 binding					
329	polyclonal (VEI1)	gp160 (131–151)	Env (131–151)	CTDLKNDTNTNSSSGRMMMEK		HIV-1 infection	human
		References Carlos1999 • Antibody response to the epitopes in a vaccine construct (VEI) containing peptides from 5 hypervariable regions of gp120 was detected in the sera of HIV-1 positive subjects, including sera from 6 non-subtype B infections – serum samples from San Francisco, Canada and Puerto Rico cohort showed presence of antibodies against all five VEI hypervariable regions, but most consistently against the V3 region peptide NNNTRKSIRIGPGRAFYTTGDIGNIRQ [Carlos1999]					
330	35D10/D2	gp160 (139–155)	gp120	NTKSSNWKEMDGEIK	L	Vaccine	human from transgenic mice (IgG2κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) **Ab type** V1 **Donor** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** He2002 • 35D10/D2: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – several of the MAbs obtained were effective at neutralizing the autologous strain – C-term-V1- region was immunodominant in these mice and the ten V1-specific MAbs could potently neutralize autologous strain SF162 but were highly type specific [He2002]					
331	40H2/C7	gp160 (139–155)	gp120	NTKSSNWKEMDGEIK	L	Vaccine	human from transgenic mice (IgG2κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) **Ab type** V1 **Donor** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References He2002					
		• 40H2/C7: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – several of the MAbs obtained were effective at neutralizing the autologous strain – C-term-V1- region was immunodominant in these mice and the ten V1-specific MAbs could potently neutralize autologous strain SF162 but were highly type specific [He2002]					
332	43A3/E4	gp160 (139–155)	gp120	NTKSSNWKEMDGEIK		Vaccine	human from transgenic mice (IgG2κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) **Ab type** V1 **Donor** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** He2002					
		• 43A3/E4: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – several of the MAbs obtained were effective at neutralizing the autologous strain – C-term-V1- region was immunodominant in these mice and the ten V1-specific MAbs could potently neutralize autologous strain SF162 but were highly type specific [He2002]					
333	43C7/B9	gp160 (139–155)	gp120	NTKSSNWKEMDGEIK	L	Vaccine	human from transgenic mice (IgG2κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) **Ab type** V1 **Donor** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** He2002					
		• 43C7/B9: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – several of the MAbs obtained were effective at neutralizing the autologous strain – C-term-V1- region was immunodominant in these mice and the ten V1-specific MAbs could potently neutralize autologous strain SF162 but were highly type specific [He2002]					
334	45D1/B7	gp160 (139–155)	gp120	NTKSSNWKEMDGEIK	L	Vaccine	human from transgenic mice (IgG2κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) **Ab type** V1 **Donor** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** He2002					
		• 45D1/B7: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – several of the MAbs obtained were effective at neutralizing the autologous strain – C-term-V1- region was immunodominant in these mice and the ten V1-specific MAbs could potently neutralize autologous strain SF162 but were highly type specific [He2002]					
335	46E3/E6	gp160 (139–155)	gp120	NTKSSNWKEMDGEIK		Vaccine	human from transgenic mice (IgG2κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) **Ab type** V1 **Donor** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References He2002					
		• 46E3/E6: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – several of the MAbs obtained were effective at neutralizing the autologous strain – C-term-V1- region was immunodominant in these mice and the ten V1-specific MAbs could potently neutralize autologous strain SF162 but were highly type specific [He2002]					
336	58E1/B3	gp160 (139–155)	gp120	NTKSSNWKEMDGEIK	L	Vaccine	human from transgenic mice (IgG2κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) **Ab type** V1 **Donor** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** He2002					
		• 58E1/B3: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – several of the MAbs obtained were effective at neutralizing the autologous strain – C-term-V1- region was immunodominant in these mice and the ten V1-specific MAbs could potently neutralize autologous strain SF162 but were highly type specific [He2002]					
337	64B9/A6	gp160 (139–155)	gp120	NTKSSNWKEMDGEIK	L	Vaccine	human from transgenic mice (IgG2κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) **Ab type** V1 **Donor** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** He2002					
		• 64B9/A6: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – several of the MAbs obtained were effective at neutralizing the autologous strain – C-term-V1- region was immunodominant in these mice and the ten V1-specific MAbs could potently neutralize autologous strain SF162 but were highly type specific [He2002]					
338	69D2/A1	gp160 (139–155)	gp120	NTKSSNWKEMDGEIK	L	Vaccine	human from transgenic mice (IgG2κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) **Ab type** V1 **Donor** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** He2002					
		• 69D2/A1: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – several of the MAbs obtained were effective at neutralizing the autologous strain – C-term-V1- region was immunodominant in these mice and the ten V1-specific MAbs could potently neutralize autologous strain SF162 but were highly type specific [He2002]					
339	82D3/C3	gp160 (139–155)	gp120	NTKSSNWKEMDGEIK		Vaccine	human from transgenic mice (IgG2κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) **Ab type** V1 **Donor** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

References He2002

- 82D3/C3: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – several of the MAbs obtained were effective at neutralizing the autologous strain – C-term-V1- region was immunodominant in these mice and the ten V1-specific MAbs could potentially neutralize autologous strain SF162 but were highly type specific [He2002]

340	2H1B	gp160 (155–161)	gp120 (370–376 HIV2ROD)	RNISFKA	no	Vaccine	murine

Vaccine *Vector/Type:* peptide *Strain:* HIV-2 ROD
Ab type C3
References Matsushita1995

- 2H1B: Binds in WB, but binds poorly to Env on the cell surface [Matsushita1995]

341	697-D (697D, 697-30D)	gp160 (161–180)	gp120 (161–180 IIIB)	ISTSIRGKVQKEYAFFYKLD	P (weak)	HIV-1 infection	human (IgG1λ)

Ab type V2 **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center) or Cellular Products Inc, Buffalo NY
References Gorny1994, Forthal1995, Moore1995b, Trkola1996a, Binley1997a, Fouts1997, Parren1997c, Nyambi1998, Stamatatos1998, Gorny2000a, Hioe2000, Nyambi2000, Edwards2002, Maksiutov2002

- 697-D: Conformational with weak reactivity to V2 peptide ISTSIRGKVQKEYAFFYKLD – neutralized 3/4 primary isolates, but none of 4 lab strains – V2 substitutions 176/177 FY/AT, 179/180 LD/DL, 183/184 PI/SG, and 192-194 YSL/GSS abrogate binding – anti-C4 MAbs G3-536 and G45-60 enhance binding – mild oxidation of carbohydrate moieties inhibits binding [Gorny1994]
- 697-D: Not neutralizing, no ADCC activity, and no viral enhancing activity [Forthal1995]
- 697-D: Review: called 697/30D – neutralizes some primary, but not lab adapted strains [Moore1995b]
- 697-D: Partial inhibition of gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study [Trkola1996a]
- 697-D: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric Env binding – 697-D bound monomer, did not bind oligomer or neutralize JRFL [Fouts1997]
- 697-D: Does not neutralize TCLA strains but neutralizes some primary isolates weakly [Parren1997c]
- 697-D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – V2 Abs 697-D, 1361, and 1357 tended to bind weakly with a similar pattern of specificity to virions, and bound well to soluble gp120: weak binding to 1/4 B clade viruses (CA5), and weak binding to viruses from subtype A and D [Nyambi1998]
- 697-D: Called 697-30D – deleting the V2 loop of neutralization-resistant HIV-1 isolate SF162 does not abrogate its replication in PBMC or macrophages, but it enhances its neutralization sensitivity to sera from patients with B clade infection up to 170-fold, and also enhances sensitivity to sera from clades A through F – deletion of V1 or V2 did not enable neutralization by V2 MAbs G3.4, G3.136, or 687-30D [Stamatatos1998]
- 697-D: Binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – V2 MAbs 697-D, 1357 and 1361 favored the monomer by approximately 2 fold[Gorny2000a]
- 697-D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – CD4BS MAbs or serum Ig from HIV+ individuals inhibited proliferative responses of gp120 specific T cells – V2 MAb 697-D did not effect proliferation [Hioe2000]
- 697-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 5 anti-V2 MAbs, which showed weak and sporadic binding, with the most frequent binding to C and D clades [Nyambi2000]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 697-D: Called 697D – Truncation of the gp41 cytoplasmic domain of X4, R5, and X4R5 viruses forces a conformation that more closely resembles the CD4 bound state of the external Envelope, enhancing binding of CD4i MAbs 17b and 48d and of CD4BS MAbs F105, b12, and in most cases of glycosylation site dependent MAb 2G12 and the anti-gp41 MAb 246D – in contrast, binding of the anti-V2 MAb 697D and the anti-V3 MAb 694/98D were not affected – viruses bearing the truncation were more sensitive to neutralization by MAbs 48d, b12, and 2G12 – the anti-C5 MAb 1331A was used to track levels of cell surface expression of the mutated proteins [Edwards2002] • 697-D: Called 697D – Transgenic mice carrying human genes allowing production of fully human MAbs were used to rapidly create a panel of anti-HIV gp120 MAb producing hybridomas by immunization with HIV SF162 gp120 – the previously described human MAbs 5145A, 4117C and 697D were used as controls [He2002] • 697-D: This epitope is similar to a fragment of the human protein macrophage colony stimulating factor I receptor SISIRLKVQK [Maksiutov2002].					
342	6C4/S	gp160 (162–169)	gp120 (BH10)	STSIRGKV		Vaccine	
		Vaccine *Vector/Type:* protein *Strain:* BH10 *HIV component:* gp120 **Donor** S. Ranjbar (NIBSC, UK) **References** Moore1993b • 6C4/S: UK Medical Research Council AIDS reagent: ARP3049					
343	C108G	gp160 (162–169)	gp120 (162–169 HXB2)	STSIRGKV	L	HIV-1 infection	chimpanzee (IgG1κ)
		Donor S. Tilley, Public Health Research Institute, NY, NY **References** Warrier1994, Wu1995, Warrier1995, Warrier1996, Ugolini1997, Mondor1998, Alsmadi1998 • C108G: Chimps were infected with HIV-1 IIIB, and this high affinity MAb gave potent neutralization of HIV-1 IIIB – binding not affected by reduction of disulfide bonds – binding disrupted by removal of N-linked glycans – peptide binding lower affinity than glycosylated Env [Warrier1994] • C108G: Strain specificity: LAI, BaL, HXB2 – conformational character – glycosylation site at 160 critical – mutation of conserved glycosylation site at 156 increased epitope exposure [Wu1995] • C108G: Characterization of MAb variable region [Warrier1995] • C108G: Synergistic neutralization of HIV-1 when combined with anti-V3 MAbs 0.5beta and C311E, or anti-CD4BS MAbs, 1125H and 5145A – neutralization further enhanced by presence of both 1125H and 0.5beta [Warrier1996] • C108G: Viral binding inhibition by C108G was correlated with neutralization (all other neutralizing MAbs tested showed some correlation except 2F5) [Ugolini1997] • C108G: Inhibits HX10 binding to both CD4 positive and negative HeLa cells[Mondor1998] • C108G: A study of 6 anti-Env MAbs and their ability to bind or direct ADCC against target cells infected with IIIB, MN, SF-2, and RF – bound and directed lysis against only IIIB – this is first demonstration of ADCC directed by a V2 specific MAb [Alsmadi1998]			
344	10/76b	gp160 (162–170)	gp120 (162–171 BH10)	STSIRGKVQ	L (HXB10)	Vaccine	rat (IgG2a)
		Vaccine *Vector/Type:* recombinant protein *Strain:* BH10 *HIV component:* gp120 **References** McKeating1993b, McKeating1993a, Shotton1995, Wu1995, McKeating1996b • 10/76b: R to L substitution abrogated binding – human sera recognize epitope [McKeating1993b] • 10/76b: Cross-competes with MAbs 10/76b and 11/4b – HXB2 neutralization escape mutant has the substitution I/T at residue 165 [Shotton1995] • 10/76b: Included in cross-competition and neutralization studies [Shotton1995] • 10/76b: HX10 strain specificity – binds native, deglycosylated, or denatured gp120 [Wu1995] • 10/76b: Neutralizes HXB2, but fails to neutralize chimeric virus with gp120 from primary isolates in an HXB2 background [McKeating1996b] • 10/76b: UK Medical Research Council AIDS reagent: ARP3077					
345	11/41e	gp160 (162–170)	gp120 (162–171)	STSIRGKVQ	L (HXB10)	Vaccine	rat (IgG1)
		Vaccine *Vector/Type:* recombinant protein *Strain:* BH10 *HIV component:* gp120					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References McKeating1993b, Shotton1995, Wu1995 • 11/41e: R to L abrogated binding – human sera recognize the epitope [McKeating1993b] • 11/41e: Included in cross-competition and neutralization studies [Shotton1995] • 11/41e: HX10 strain specificity – binds native and deglycosylated gp120 [Wu1995]					
346	11/4b	gp160 (162–170)	gp120 (162–171)	STSIRGKVQ	L (HXB10)	Vaccine	rat (IgG2a)
		Vaccine *Vector/Type:* recombinant protein *Strain:* BH10 *HIV component:* gp120 **References** McKeating1993b, Shotton1995, Wu1995, Moore1996 • 11/4b: A change from R to L abrogated binding – human sera recognize epitope [McKeating1993b] • 11/4b: Cross-competes with MAbs 10/76b and 11/4c – HXB2 neutralization escape mutant has the substitution I/T at residue 165 [Shotton1995] • 11/4b: HXB10 strain specificity – binds native, deglycosylated, or denatured gp120 [Wu1995] • 11/4b: Linear V2 epitope – reciprocal binding enhancement of anti-V2 discontinuous epitope antibodies (in contrast to BAT085) and CD4 inducible antibody 48d. Reciprocal inhibits BAT085 binding – inhibits CRA-3 binding CRA-3 does not inhibit 11/4b [Moore1996]					
347	RSD-33	gp160 (162–170)	gp120 (162–171)	STSIRGKVQ		Vaccine	
		Vaccine *Vector/Type:* protein *Strain:* BH10 *HIV component:* gp120 **Donor** R. Daniels (NIMR, UK) **References** Moore1993b					
348	11/4c (11/4c/1j/4j)	gp160 (162–170)	gp120 (152–181)	STSIRGKVQ	L (HXB2)	Vaccine	rat (IgG2a)
		Vaccine *Vector/Type:* recombinant protein *Strain:* BH10 *HIV component:* gp120 **Ab type** V2 **References** McKeating1993b, Wu1995, Shotton1995, Peet1998 • 11/4c: R to L substitution abrogated binding – human sera recognize epitope [McKeating1993b] • 11/4c: HX10 strain specificity – binds native, deglycosylated, or denatured gp120 [Wu1995] • 11/4c: Cross-competes with MAbs 10/76b and 11/4b – HXB2 neutralization escape mutant has the substitution I/T at residue 165 [Shotton1995] • 11/4c: Called 11/4c/1j/4j – The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind – 11/4c was not affected by V3 serine substitutions – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions [Peet1998] • 11/4c: UK Medical Research Council AIDS reagent: ARP3035					
349	8.22.2	gp160 (162–178)	gp120	TTSIRDKVQKEYALFYK		Vaccine	human from transgenic mice (IgG2κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) **Ab type** V2 **Donor** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** He2002, Maksiutov2002 • 8.22.2 : Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – several of the MAbs obtained were effective at neutralizing the autologous strain – 8.22.2 was the only V2-specific MAb created and it could cross-compete with MAb 697D – 8.22.2 could cross-react with BaL and JR-FL, two B clade R5 strains, but not B clade X4 or E clade viruses, and it could weakly neutralize autologous strain SF162 [He2002] • 8.22.2: This epitope is similar to a fragment of the human protein macrophage colony stimulating factor I receptor SISIRLKVQK [Maksiutov2002].					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
350	12b	gp160 (162–181)	gp120 (162–181)	STSIRGKVQKEYAFFYKLDI	L (HXB10)	Vaccine	rat (IgG2a)

Vaccine *Vector/Type:* recombinant protein *Strain:* BH10 *HIV component:* gp120
Ab type V2
References Shotton1995, McKeating1996b, Maksiutov2002

- 12b: V2 MAb neutralized HXB2 – position 179-180 LD to DL abrogates binding – competes with 60b, but not 74 [Shotton1995]
- 12b: Neutralizes HXB2, but fails to neutralize chimeric virus with gp120 from primary isolates in an HXB2 background [McKeating1996b]
- 12b: This epitope is similar to a fragment of the human protein macrophage colony stimulating factor I receptor SISIRLKVQK [Maksiutov2002].

351	G3-136 (G3.136)	gp160 (170–180)	gp120 (170–180 IIIB)	QKEYAFFYKLD	L	Vaccine	murine (IgG)

Vaccine *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* gp120
Ab type V2 **Donor** Tanox Biosystems Inc and David Ho, ADARC, NY
References Fung1992, Pirofski1993, Thali1993, Moore1993a, Moore1993b, Yoshiyama1994, Sattentau1995b, Stamatatos1995, Moore1996, Poignard1996a, Binley1997a, Stamatatos1997, Ditzel1997, Wyatt1997, Parren1998a, Stamatatos1998, Ly2000

- G3-136: V2 region – binds and neutralizes IIIB and RF in CEM-SS cells, but not MN – neutralization activity against a few primary isolates in PBMC – sCD4 binding inhibits binding (contrast with BAT085) – deglycosylation or reduction of gp120 by DTT diminishes reactivity [Fung1992]
- G3-136: Conformational, does not bind well to denatured gp120 – not reactive with SF-2 gp120, and does not inhibit HIV-1 sera from binding to IIIB gp120 [Moore1993a]
- G3-136: Marginal binding to peptide, binding inhibited by 183/184 PI/SG substitution [Moore1993b]
- G3-136: Binding enhanced by selected antibodies to C1, C4, C5, V3 and anti-CD4 binding site MAbs – enhances binding of selected V3, C4 and anti-CD4 binding site MAbs [Moore1993b]
- G3-136: HIV-1 RF V2 substitutions 177 Y/H and 179 L/P in the V2 loop of RF reduce affinity [Yoshiyama1994]
- G3-136: The binding of conformation-dependent anti-V2, anti-V3, and anti-CD4BS MAbs to monomeric and virion-associated gp120 from HIV-1 isolates with differences in cell tropism was studied – V2 loop epitopes are somewhat occluded in the oligomeric gp120 epitopes on the virion surface relative to the gp120 monomer as indicated by an increase in the half-maximal binding values to macrophage-tropic isolates SF162 and SF128a – anti-V2 MAbs G3-4 and G3.136 don't bind to T-cell tropic SF2 [Stamatatos1995]
- G3-136: Bound preferentially to the monomeric rather than oligomeric form of LAI gp120 – neutralizes cell free Hx10 [Sattentau1995b]
- G3-136: Described epitope as STSIRGKVKEYAFFYKLDI – binds oligomer – binding of V2 MAbs G3-136, G3-4 or BAT123 did not significantly alter gp120 dissociation from virus or expose the gp41 epitope of MAb 50-69, in contrast to anti-V3 MAbs [Poignard1996a]
- G3-136: Called G3.136 – does not mediate gp120 virion dissociation in contrast to anti-V2 MAb G3-4 – not neutralizing for SF162 or SF128A in either primary macrophages or PBMC [Stamatatos1997]
- G3-136: Binds both gp120 and soluble gp120+gp41 complex efficiently, suggesting its gp120 epitope is not blocked by gp41 binding [Wyatt1997]
- G3-136: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren1998a]
- G3-136: Called G3.136 – deleting the V2 loop of neutralization-resistant HIV-1 isolate SF162 does not abrogate its replication in PBMC or macrophages, but it enhances its neutralization sensitivity to sera from patients with B clade infection up to 170-fold, and also enhances sensitivity to sera from clades A through F – deletion of V1 or V2 did not enable neutralization by V2 MAbs G3.4, G3.136, or 687-30D [Stamatatos1998]
- G3-136: Called G3.136 – SF162 is a neutralization-resistant HIV-1 isolate – N-linked glycosylation modifications in the V2 loop of the SF162 gp120 revealed that these sites prevent neutralization by CD4BS MAbs (IgG1b12 and IgGCD4), and protect against neutralization by V3 MAbs (447-D and 391-95D) – V2-region glycosylation site mutations did not alter neutralization resistance to V2 MAbs (G3.4 and G3.136) or CD4i MAbs (17b and 48d) – V2 glycosylation site modification allows infection of macrophages, probably due to glycosylated forms requiring fewer CCR5 molecules for viral entry [Ly2000]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
352	G3-4 (G3.4)	gp160 (170–180)	gp120 (170–180 BH10)	QKEYAFFYKLD	L	Vaccine	murine (IgG2bκ)

Vaccine *Vector/Type:* protein *Strain:* IIIB *HIV component:* gp120
Ab type V2 **Donor** Tanox Biosystems Inc and David Ho, ADARC, NY
References Ho1991a, Ho1992, Fung1992, McKeating1992a, Moore1993a, Sullivan1993, Sattentau1993, Thali1993, Moore1993b, Moore1994b, Gorny1994, Thali1994, Yoshiyama1994, Stamatatos1995, Wu1995, Sattentau1995b, Jagodzinski1996, Moore1996, Poignard1996a, Binley1997a, Stamatatos1997, Ditzel1997, Wyatt1997, Parren1998a, Stamatatos1998, Ly2000, Srivastava2002

- G3-4: Binding is sensitive to removal of glycans by endo H – 50% neutralization of 4/9 primary isolates – has conformational features [Ho1991a]
- G3-4: Neutralizes IIIB and RF, not MN – blocks sCD4-gp120, not as potent as MAb 15e – V2 binding MAbs BAT085 and G3-136 block G3-4 gp120 binding – sensitive to reduction of gp120 by DTT [Ho1992]
- G3-4: Substitutions in residues 176 to 184 affect MAb recognition – substitutions in V2 can result in gp120-gp41 dissociation [Sullivan1993]
- G3-4: Increased binding in the presence of sCD4 [Sattentau1993]
- G3-4: Conformational, does not bind well to denatured gp120 – not reactive with SF-2 gp120, and does not inhibit HIV-1 sera from binding to IIIB gp120 [Moore1993a]
- G3-4: V2 region, marginal binding to peptide, binding inhibited by 183/184 PI/SG substitution [Moore1993b]
- G3-4: Conformationally sensitive – sporadic cross-reactivity among, and outside, B clade gp120s [Moore1994b]
- G3-4: Weakly neutralizing, IC 50 = 53 mug/ml [Gorny1994]
- G3-4: gp41 mutation (582 A/T) that reduces neutralization of anti-CD4 binding site MAbs does not alter G3-4s ability to neutralize [Thali1994]
- G3-4: Neutralizes RF – substitutions 177 Y/H and 179 L/P in the V2 loop of RF reduce affinity and result in neutralization escape [Yoshiyama1994]
- G3-4: The binding of conformation-dependent anti-V2, anti-V3, and anti-CD4BS MAbs to monomeric and virion-associated gp120 from HIV-1 isolates with differences in cell tropism was studied – V2 loop epitopes are somewhat occluded in the oligomeric gp120 epitopes on the virion surface relative to the gp120 monomer as indicated by an increase in the half-maximal binding values to macrophage-tropic isolates SF162 and SF128a – anti-V2 MAbs G3-4 and G3.136 don't bind to T-cell tropic SF2 [Stamatatos1995]
- G3-4: Reactive with BH10, RF, and MN – binds native, but not denatured or deglycosylated gp120, binds to deglycosylated V1V2 fusion protein, suggesting importance of glycans outside the V1V2 region [Wu1995]
- G3-4: Bound preferentially to the monomeric rather than oligomeric form of LAI gp120 – neutralizes Hx10 cell-free virus [Sattentau1995b]
- G3-4: The sulfated polysaccharide curdlan sulfate (CRDS) binds to the Envelope of T-tropic viruses and neutralizes virus – deletion of the V3 loop from gp120 results in more potent G3-4 binding inhibition by CRDS – G3-4 epitope described as 176-184 FYKLDIIPI and 191-193 YSL [Jagodzinski1996]
- G3-4: Binding enhanced by selected antibodies to C1, C4, C5, V3 and anti-CD4 binding site MAbs – enhances binding of selected V3, C4 and anti-CD4 binding site MAbs [Moore1996]
- G3-4: Described epitope as STSIRGKVKEYAFFYKLDI – binds oligomer – binding of V2 MAbs G3-136, G3-4 or BAT085 did not significantly alter gp120 dissociation from virus or expose the gp41 epitope of MAb 50-69, in contrast to anti-V3 MAbs [Poignard1996a]
- G3-4: Called G3.4 – mediates gp120 virion dissociation in contrast to anti-V2 MAb G3-136 – not neutralizing for SF162 or SF128A in either primary macrophages or PBMC [Stamatatos1997]
- G3-4: Binds both gp120 and soluble gp120+gp41 complex efficiently, suggesting its gp120 epitope is not blocked by gp41 binding [Wyatt1997]
- G3-4: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren1998a]
- G3-4: Called G3.4 – Deleting the V2 loop of neutralization-resistant HIV-1 isolate SF162 does not abrogate its replication in PBMC or macrophages, but it enhances its neutralization sensitivity to sera from patients with B clade infection up to 170-fold, and also enhances sensitivity to sera from clades A through F – deletion of V1 or V2 did not enable neutralization by V2 MAbs G3.4, G3.136, or 687-30D [Stamatatos1998]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• G3-4: Called G3.4 – SF162 is a neutralization-resistant HIV-1 isolate – N-linked glycosylation modifications in the V2 loop of the SF162 gp120 revealed that these sites prevent neutralization by CD4BS MAbs (IgG1b12 and IgGCD4), and protect against neutralization by V3 MAbs (447-D and 391-95D) – V2-region glycosylation site mutations did not alter neutralization resistance to V2 MAbs (G3.4 and G3.136) or CD4i MAbs (17b and 48d) – V2 glycosylation site modification allows infection of macrophages, probably due to glycosylated forms requiring fewer CCR5 molecules for viral entry [Ly2000] • G3-4: Called G3.4 – Oligomeric gp140 (o-gp140) derived from R5 primary isolate US4 was characterized for use as a vaccine reagent – antigen capture ELISA was used to compare the antigenicity of gp120 and o-gp140 using a panel of well characterized MAbs – G3.4 recognized o-gp140 [Srivastava2002]					
353	BAT085 (BAT-085)	gp160 (171–180)	gp120 (170–180 IIIB)	KEYAFFYKLD	L	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* inactivated virus *Strain:* IIIB *HIV component:* virus **Donor** Tanox Biosystems Inc and David Ho, ADARC, NY **References** Fung1987, Fung1992, Moore1993a, Pirofski1993, Thali1993, Moore1993b, D'Souza1994, Moore1994d, Gorny1994, Yoshiyama1994, Wu1995, Sattentau1995b, Moore1996, Poignard1996a, Binley1997a, Ditzel1997, Parren1998a • BAT085: V2 region – sCD4 does not block – neutralizes IIIB and some primary isolates, but not MN or RF – binds MN – deglycosylation or DDT reduction of gp120 does not diminish reactivity [Fung1992] • BAT085: Called BAT-85 – conformational, does not bind well to denatured gp120 – not reactive with SF-2 gp120, and does not inhibit HIV-1 sera from binding to IIIB gp120 [Moore1993a] • BAT085: 7/8 V2 murine MAbs required gp120 native structure to bind, but BAT085 was the exception – type-specific [Moore1993b] • BAT085: Peptide affinities of G3-136 and G3-4 are 100-fold less than BAT085, but BAT085 has lower affinity for BH10 gp120 and is weaker at neutralization [Moore1993b] • BAT085: Multi-lab study for antibody characterization and assay comparison – did not bind MN or SF2 [D'Souza1994] • BAT085: Interacts with two overlapping peptides with region of overlap KEYAFFYKLD [Gorny1994] • BAT085: Neutralizes RF – substitution 177 Y/H in the V2 loop of RF does not inhibit neutralization, in contrast to MAbs G3-4 and SC258 [Yoshiyama1994] • BAT085: HXB10 strain specificity – binds native, deglycosylated, or denatured gp120 [Wu1995] • BAT085: Bound preferentially to the monomeric rather than oligomeric form of LAI gp120 – neutralizes cell free Hx10 [Sattentau1995b] • BAT085: Binding is blocked by other V2 region antibodies, enhanced by several anti-C1 MAbs, and anti-V3 MAb G511 – reciprocal enhancement of CD4i MAb 48d binding [Moore1996] • BAT085: Epitope suggested to be QKEYAFFYKLD – binds oligomer – binding of V2 MAbs G3-136, G3-4 or BAT123 did not significantly alter gp120 dissociation from virus or expose the gp41 epitope of MAb 50-69, in contrast to anti-V3 MAbs [Poignard1996a] • BAT085: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren1998a]					
354	60b	gp160 (172–181)	gp120 (172–181 HXB2)	EYAFFYKLDI	no	Vaccine	rat (IgG2b)
		Vaccine *Vector/Type:* recombinant protein *Strain:* BH10 *HIV component:* gp120 **References** Shotton1995 • 60b: V2 MAb did not neutralize HXB2 – bound to rgp120 in ELISA – substitutions 179-180 LD/DL and 191-193 YSL/GSS abrogate binding, as do changes outside the minimum epitope – competes with 12b, but not 74 [Shotton1995]					
355	74	gp160 (172–181)	gp120 (172–181)	EYAFFYKLDI	no	Vaccine	rat (IgG1)
		Vaccine *Vector/Type:* recombinant protein *Strain:* BH10 *HIV component:* gp120 **References** Shotton1995					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 74: V2 MAb did not neutralize HXB2 – did not bind rgp120 ELISA – position 179-180 LD to DL abrogates binding, as do changes outside the minimum epitope – does not compete with 60b or 12b, and is enhanced by two conformation dependent MAbs [Shotton1995]					
356	38/12b	gp160 (172–191)	gp120 (172–191 HXB2)	EYAFFYKLDIIPIDNDTTSY		Vaccine	rat
		Vaccine *Vector/Type:* protein *Strain:* BH10 *HIV component:* gp120 **References** Wu1995 • 38/12b: Broad specificity: HXB2, MN, SF162 – binds native and deglycosylated gp120 [Wu1995]					
357	38/60b	gp160 (172–191)	gp120 (172–191 HXB2)	EYAFFYKLDIIPIDNDTTSY		Vaccine	rat
		Vaccine *Vector/Type:* protein *Strain:* BH10 *HIV component:* gp120 **References** Wu1995 • 38/60b: Strain specificity: HXB2 – binds native and deglycosylated gp120 [Wu1995]					
358	polyclonal (VEI2)	gp160 (176–196)	Env	FYKLDIVPIDNTTTSYRLISC		HIV-1 infection	human
		References Carlos1999 • Antibody response to the epitopes in a vaccine construct (VEI) containing peptides from 5 hypervariable regions of gp120 was detected in the sera of HIV-1 positive subjects, including sera from 6 non-subtype B infections – serum samples from San Francisco, Canada and Puerto Rico cohort showed presence of antibodies against all five VEI hypervariable regions, but most consistently against the V3 region peptide NNNTRKSIRIGPGRAFYTTGDIGNIRQ [Carlos1999]					
359	322-151	gp160 (211–221)	gp120 (201–220 LAI)	EPIPIHYCAPA		Vaccine	murine (IgG)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Env **Donor** G. Robey, Abbot Labs **References** Moore1994c, Moore1994d • 322-151: The relative affinity denatured/native gp120 is 30 [Moore1994c]					
360	3D3.B8	gp160 (211–221)	gp120 (211–220 LAI)	EPIPIHYCAPA		Vaccine	murine (IgG)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Env **References** Bolmstedt1990, Moore1994c • 3D3.B8: The relative affinity denatured/native gp120 is greater than 10 [Moore1994c]					
361	4C11.D8	gp160 (211–221)	gp120 (211–220 LAI)	EPIPIHYCAPA		Vaccine	murine (IgM)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Env **References** Bolmstedt1990, Moore1994c • 4C11.D8: The relative affinity denatured/native gp120 is greater than 10 [Moore1994c]					
362	493-156	gp160 (211–230)	gp120 (211–230 LAI)	EPIPIHYCAPAGFAILKCNN		Vaccine	murine (IgG)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Env **Donor** G. Robey, Abbot Labs **References** Moore1994c • 493-156: The relative affinity denatured/native gp120 is >10 [Moore1994c]					
363	110.1	gp160 (212–221)	gp120 (200–217)	PIPIHYCAPA	no	Vaccine	human
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Env **References** Pincus1993a, Pincus1996, Valenzuela1998 • 110.1: There is another antibody with this ID that binds to Env at positions 491-500 in LAI, see [Gosting1987]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 110.1: A panel of immunotoxins were generated by linking Env MAbs to ricin A – immunotoxins mediated cell killing, but killing was not directly proportional to binding – 110.1-RAC did not mediate cell killing, and sCD4 has no effect [Pincus1993a, Pincus1996]					
364	GV4H3	gp160 (219–226)	gp120 (219–226 IIIB)	APAGFAIL		Vaccine	murine
		Vaccine *Vector/Type:* protein-Ab complex *HIV component:* gp120 complexed with MAb M77 **References** Denisova1996 • GV4H3: When anti-V3 MAb M77 was bound to gp120 and used as an immunogen, it stimulated many MAbs to linear epitopes [Denisova1996]					
365	J1	gp160 (222–231)	gp120 (222–231 LAI)	GFAILKCNNK		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* peptide *Strain:* LAI **Donor** J. Hoxie, U. Penn. **References** Moore1994c, Moore1994d, Cook1994 • J1: The relative affinity denatured/native gp120 is 30 [Moore1994c] • J1: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – MAbs against the N-terminal half of gp120 do not inhibit gp120 binding to GalCer – binding of GalCer to gp120 does not inhibit MAb binding [Cook1994]					
366	J3	gp160 (222–231)	gp120 (222–231 LAI)	GFAILKCNNK		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* peptide *Strain:* LAI **Donor** J. Hoxie, U. Penn. **References** Moore1994c, Cook1994 • J3: The relative affinity denatured/native gp120 is 30 [Moore1994c] • J3: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – MAbs against the N-terminal half of gp120 do not inhibit gp120 binding to GalCer – binding of GalCer to gp120 does not inhibit MAb binding [Cook1994]					
367	1006-30-D	gp160 (236–245)	gp120 (241–251)	KGSCKNVSTV			human (IgG1λ)
		Ab type C2 **References** Hioe2000, Nyambi2000 • 1006-30-D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – CD4BS MAbs or serum Ig from HIV+ individuals inhibited proliferative responses of gp120 specific T cells – C2 MAbs 1006-30-D and 847-D did not effect proliferation [Hioe2000] • 847-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including two C2 MAbs – the binding of anti-C2 MAbs was weak to isolates from clades B, C, D, E, F, G, and they did not not bind to isolates from subtypes A and H – epitope is suggested to be in a 20 amino acid peptide KGSCKNVSTVQCTHGIRPVV [Nyambi2000]					
368	847-D	gp160 (236–245)	gp120 (241–251)	KGSCKNVSTV			human (IgG1λ)
		Ab type C2 **References** Hioe2000, Nyambi2000 • 847-D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – CD4BS MAbs or serum Ig from HIV+ individuals inhibited proliferative responses of gp120 specific T cells – C2 MAbs 1006-30-D and 847-D did not effect proliferation [Hioe2000] • 847-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including two C2 MAbs – the binding of anti-C2 MAbs was weak to isolates from clades B, C, D, E, F, G, and they did not not bind to isolates from subtypes A and H – epitope is suggested to be in a 20 amino acid peptide KGSCKNVSTVQCTHGIRPVV [Nyambi2000]					
369	MF169.1	gp160 (252–261)	gp120 (242–261 LAI)	RPVVSTQLLL		Vaccine	murine (IgG)
		Vaccine *Strain:* LAI *HIV component:* Env					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Thiriart1989, Moore1994c, Moore1994d • MF169.1: The relative affinity denatured/native gp120 is 11 – mutations 252 R/W, 257 T/G, and 257 T/R impair binding [Moore1994c]					
370	MF170.1	gp160 (252–261)	gp120 (242–261 LAI)	RPVVSTQLLL		Vaccine	murine (IgG)
		Vaccine *Strain:* LAI *HIV component:* Env **References** Thiriart1989, Moore1994c, Moore1994d • MF170.1: The relative affinity denatured/native gp120 is 15 – mutations 252 R/W, 257 T/G, and 257 T/R impair binding to denatured and native gp120, and 262N/T, 269 E/L and 281 A/V to only native gp120 [Moore1994c]					
371	MF87.1	gp160 (252–261)	gp120 (242–261 LAI)	RPVVSTQLLL		Vaccine	murine (IgG)
		Vaccine *Strain:* LAI *HIV component:* Env **References** Thiriart1989, Moore1994c • MF87.1: The relative affinity denatured/native gp120 is 10 – mutations 252 R/W, 257 T/G, and 257 T/R impair binding [Moore1994c]					
372	213.1	gp160 (252–261)	gp120 (242–261 LAI)	RPVVSTQLLL		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Env **Ab type** C2 **Donor** Claudine Bruck **References** Thiriart1989, Moore1993a, Moore1994c • 213.1: Bound preferentially to denatured IIIB and SF2 gp120 [Moore1993a] • 213.1: The relative affinity denatured/native gp120 is 100 – mutations 252 R/W, 257 T/G or T/R impair binding [Moore1994c] • 213.1: UK Medical Research Council AIDS reagent: ARP334					
373	B12	gp160 (252–271)	gp120 (252–271 LAI)	RPVVSTQLLLNGSLAEEEVV		Vaccine	murine (IgG)
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* gp160 **Ab type** C2 **References** Moore1994c, Maksiutov2002 • B12: C2 region – the relative affinity for denatured/native gp120 is 27 – mutations 257 T/R and 262 N/T impair binding [Moore1994c] • B12: This epitope is similar to a fragment of human protein lymphatic endothelium-specific hyaluronan receptor LYVE-1, TTRLLVQGSLRAEE [Maksiutov2002].					
374	B13 (Bh13, Chessie B13)	gp160 (252–271)	gp120 (252–271 LAI)	RPVVSTQLLLNGSLAEEEVV		Vaccine	murine (IgG2a)
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* gp160 **Ab type** C2 **Donor** George Lewis, Institute of Human Virology, Baltimore MD, USA **References** Pincus1993a, Moore1993a, Moore1994c, Abacioglu1994, Moore1994d, Pincus1996, Connor1998, Wang2002b, Maksiutov2002 • B13: Bound preferentially to denatured IIIB gp120 [Moore1993a] • B13: The relative affinity for denatured/native gp120 is 30 – mutations 257 T/R and 269 E/L impair binding [Moore1994c] • B13: C2 region – epitope boundaries mapped by peptide scanning, core epitope: TQLLLN [Abacioglu1994] • B13: Called Bh13 – binds to gp120 but not to infected cells – when linked to ricin A, the immunotoxin did not mediate cell killing – sCD4 has no effect [Pincus1993a, Pincus1996] • B13: This epitope is similar to a fragment of human protein lymphatic endothelium-specific hyaluronan receptor LYVE-1, TTRLLVQGSLRAEE [Maksiutov2002].					
375	C13	gp160 (252–271)	gp120 (252–271 LAI)	RPVVSTQLLLNGSLAEEEVV		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* gp160 **Ab type** C2 **Donor** George Lewis					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Moore1993a, Moore1994c, Abacioglu1994, Maksiutov2002 • C13: Bound preferentially to denatured IIIB gp120 [Moore1993a] • C13: The relative affinity for denatured/native gp120 is 36 – mutations 257 T/R, 267 E/L, and 269 E/L impair binding [Moore1994c] • C13: Epitope boundary extended to RPVVSTQLLLNGSLAEEEVVIR, to take into account the effect of a point mutation [Abacioglu1994] • C13: This epitope is similar to a fragment of human protein lymphatic endothelium-specific hyaluronan receptor LYVE-1, TTRLLVQGSLRAEE [Maksiutov2002]. • C13: NIH AIDS Research and Reference Reagent Program: 1209				
376	M89	gp160 (252–271)	gp120 (252–271 LAI)	RPVVSTQLLLNGSLAEEEVV	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* Env **Ab type** C2 **Donor** Fulvia di Marzo Veronese **References** diMarzo Veronese1992, Moore1994c, Moore1994d, Maksiutov2002 • M89: Immunoblot reactive, RIP negative, for strains IIIB, 451, MN, RF, and RUTZ [diMarzo Veronese1992] • M89: C2 region – the relative affinity for denatured/native gp120 is >30 – mutations 257 T/R and 269 E/L impair binding [Moore1994c] • M89: This epitope is similar to a fragment of human protein lymphatic endothelium-specific hyaluronan receptor LYVE-1, TTRLLVQGSLRAEE [Maksiutov2002].				
377	B21	gp160 (257–262)	gp120 (257–262 BH10)	TQLLLN		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* gp160 **Ab type** C2 **References** Abacioglu1994 • B21: C2 region, epitope boundaries mapped by peptide scanning [Abacioglu1994]					
378	B23	gp160 (257–262)	gp120 (257–262 BH10)	TQLLLN		Vaccine	murine (IgG2a)
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* gp160 **Ab type** C2 **References** Abacioglu1994 • B23: C2 region, epitope boundaries mapped by peptide scanning [Abacioglu1994]					
379	B24	gp160 (257–262)	gp120 (257–262 BH10)	TQLLLN		Vaccine	murine (IgG2a)
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* gp160 **Ab type** C2 **References** Abacioglu1994 • B24: C2 region, epitope boundaries mapped by peptide scanning [Abacioglu1994]					
380	B25	gp160 (257–262)	gp120 (257–262 BH10)	TQLLLN		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* gp160 **Ab type** C2 **References** Abacioglu1994 • B25: C2 region, epitope boundaries mapped by peptide scanning [Abacioglu1994]					
381	B3	gp160 (257–262)	gp120 (257–262 BH10)	TQLLLN		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* gp160 **Ab type** C2 **References** Abacioglu1994					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• B3: C2 region, epitope boundaries mapped by peptide scanning [Abacioglu1994]					
382	B26	gp160 (257–263)	gp120 (257–263 BH10)	TQLLLNG		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* gp160 **Ab type** C2 **References** Abacioglu1994 • B26: C2 region, epitope boundaries mapped by peptide scanning [Abacioglu1994]					
383	B29	gp160 (257–263)	gp120 (257–263 BH10)	TQLLLNG		Vaccine	murine (IgG2a)
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* gp160 **Ab type** C2 **References** Abacioglu1994 • B29: C2 region, epitope boundaries mapped by peptide scanning [Abacioglu1994]					
384	B36	gp160 (257–263)	gp120 (257–263 BH10)	TQLLLNG		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* gp160 **Ab type** C2 **References** Abacioglu1994 • B36: C2 region, epitope boundaries mapped by peptide scanning [Abacioglu1994]					
385	110.E	gp160 (262–281)	gp120 (262–281 LAI)	NGSLAEEEVVIRSVNFTDNA		Vaccine	murine (IgG)
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* Env **Ab type** C2 **Donor** F. Traincard **References** Moore1994c, Moore1994d, Maksiutov2002 • 110.E: The relative affinity for denatured/native gp120 is 7.3 [Moore1994c] • 110.E: This epitope is similar to a fragment of human protein lymphatic endothelium-specific hyaluronan receptor LYVE-1, TTRLLVQGSLRAEE [Maksiutov2002].					
386	110.C	gp160 (271–280)	gp120 (271–280 LAI)	VIRSVNFTDN		Vaccine	murine (IgG)
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* Env **Ab type** C2 **Donor** F. Traincard, Hybridolabs, Institut Pasteur **References** Moore1994c, Moore1994d, Valenzuela1998 • 110.C: The relative affinity for denatured/native gp120 is 1 [Moore1994c] • 110.C: Only slightly reduces LAI viral binding or entry into CEM cells [Valenzuela1998]					
387	IIIB-V3-26	gp160 (291–307)	gp120 (299–304 IIIB)	SVEINCTRPNNNTRKSI	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* peptide *Strain:* IIIB **Ab type** V3 **References** Laman1992, Maksiutov2002 • IIIB-V3-26: Binds to the base of the V3 loop on denatured gp120 [Laman1992] • IIIB-V3-26: This epitope is similar to a fragment of the FasI receptor precursor (Apptosis-mediating surface antigen fas) (APO- 1 antigen) (CD95 antigen), VEINCTRQN [Maksiutov2002]					
388	IIIB-V3-21 (V3-21)	gp160 (294–299)	gp120 (299–304 IIIB)	INCTRP	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* peptide *Strain:* IIIB					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		Ab type V3 **Donor** J. Laman **References** Laman1992, Laman1993, Valenzuela1998, Zhang2002, Maksiutov2002 • IIIB-V3-21: Binds to the base of the V3 loop on denatured gp120 [Laman1992] • IIIB-V3-21: Binds to NP40 treated gp120, and epitope is probably obscured by local glycosylation [Laman1993] • IIIB-V3-21: Does not block HIV-1 LAI binding or entry into CEM cells [Valenzuela1998] • IIIB-V3-21: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain [Zhang2002] • IIIB-V3-21: This epitope is similar to a fragment of the FasI receptor precursor (Apptosis-mediating surface antigen fas) (APO- 1 antigen) (CD95 antigen), VEINCTRQN [Maksiutov2002] • IIIB-V3-21: UK Medical Research Council AIDS reagent: ARP3048 • IIIB-V3-21: NIH AIDS Research and Reference Reagent Program: 1725			
389	polyclonal	gp160 (296–327)	gp120 (MN)	CNYNKRKRIHIGPGRAFYTTKNIIG-TIC	L		rabbit (IgA, IgG)
		Ab type V3 **References** FitzGerald1998 • Polyclonal response to MN, or Thai E V3 loop inserted into Pseudomonas Exotoxin for vaccination – inserts of 14 or 26 amino acids were used from MN or a Thai E strain, constrained by disulfide bond – sera from vaccinated rabbit were reactive with strain-specific gp120 – administration to mucosal surfaces elicits IgA [FitzGerald1998]					
390	polyclonal	gp160 (297–330)	Env (303–335 LAI)	TRPNNNTRKSIHIGPGRAFYATGEI-IGDIRQAH	no	Vaccine	human (IgG)
		Vaccine *Vector/Type:* lipopeptide *Strain:* LAI *HIV component:* V3 *Adjuvant:* QS21 **Ab type** V3 **References** Pialoux2001 • 28 subjects were vaccinated with six HIV-1 peptides that were selected to be particularly rich in CTL epitopes, presented in lipopeptides with or without adjuvant QS21 – HIV-specific Ab responses were detected in 25/28 (89%), proliferative in 19/28 (79%), and CTL in 13/24 (54%) of testable volunteers – 14/28 had non-neutralizing Ab responses to this peptide (E), 7/24 had proliferative responses, and multiple CTL responses were detected [Pialoux2001]					
391	MO97/V3	gp160 (299–308)	gp120 (299–308 IIIB)	PNNNTRKSIR	no	in vitro stimulation	human (IgM)
		Ab type V3 **References** Ohlin1992 • MO97: Generated through in vitro stimulation of uninfected-donor lymphocytes with rpB1 (IIIB Env 286-467) [Ohlin1992]					
392	polyclonal	gp160 (299–331)	gp120 (306–338 BH10)	PNNNTRKSIRIQRGPGRAFVTIGKI-GNMRQAHC	L	Vaccine	rabbit (IgG)
		Vaccine *Vector/Type:* peptide *Strain:* BH10 **Ab type** V3 **References** Neurath1990 • 21 V3 loop variant peptides spanning this region were tested and serological cross-reactivity correlated with divergence [Neurath1990]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
393	55/1l	gp160 (300–315)	gp120 (300–315)	NNNTRKRIRIQRGPGR?			
		Ab type V3 **References** Peet1998 • 55/1l: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind, and anti-V3 MAb 55/1l binding was abrogated by V3 serine substitutions in the V3 loop – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions [Peet1998]					
394	8/38c (8/38/1c)	gp160 (300–315)	gp120 (300–315 HXB10)	NNNTRKRIRIQRGPGR	L	Vaccine	rat (IgG2a)
		Vaccine *Vector/Type:* recombinant protein *Strain:* BH10 *HIV component:* gp120 **Ab type** V3 **Donor** C. Dean and C. Shotton, Institute for Cancer Research, Surrey, UK **References** McKeating1992a, Sattentau1995b, Jeffs1996, Parren1998a, Peet1998 • 8/38c: Binds to virion gp120 and neutralizes only in the presence of sCD4 [McKeating1992a] • 8/38c: Binds equally well to monomer and oligomer, less rapid association rate than other anti-V3 antibodies, and an associated less potent neutralization of lab strains [Sattentau1995b] • 8/38c: Deletion of the V1V2 regions did not affect anti-V3 Abs ability to bind when compared to intact rec gp120 [Jeffs1996] • 8/38c: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren1998a] • 8/38c: Called 8/38/1c: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind, and anti-V3 MAb 8/38c binding was only diminished by V3 serine substitutions C-term to the tip of the loop – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions [Peet1998] • 8/38c: UK Medical Research Council AIDS reagent: ARP3039			
395	8/64b	gp160 (300–315)	gp120 (300–315 HXB10)	NNNTRKRIRIQRGPGR	L	Vaccine	rat (IgM)
		Vaccine *Vector/Type:* recombinant protein *Strain:* BH10 *HIV component:* gp120 **Ab type** V3 **References** McKeating1992a, Peet1998 • 8/64b: Binds to virion gp120 and neutralizes only in the presence of sCD4 [McKeating1992a] • 8/64b: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind, and anti-V3 MAb 8/64b binding was abrogated by V3 serine substitutions C-term to the tip of the loop – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions [Peet1998] • 8/64b: UK Medical Research Council AIDS reagent: ARP3036			
396	polyclonal	gp160 (300–321)	gp120	NYNKRKRIHIGPGRAFYTTK	L	HIV-1 infection, Vaccine	human
		Vaccine *Vector/Type:* peptide *Strain:* cocktail *HIV component:* V3 **Ab type** V3 **References** Bartlett1998					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• V3 peptide vaccine (MN, RF, EV91, and Can0A) with a C4 helper T cell epitope were used to vaccinate HLA-B7 HIV-infected patients – V3 Ab levels and the anti-HIV proliferative response, but no decrease in HIV-1 RNA levels or increase in CD4 levels was observed [Bartlett1998]					
397	polyclonal	gp160 (300–321)	gp120	NYNKRKRIHIGPGRAFYTTK		HIV-1 exposed seronegative	human (IgA)
		Ab type V3 **References** Kaul1999 • HIV-1 Env-specific mucosal IgA found in genital track of 16/21 HIV-1 resistant chronically exposed Kenyan sex workers – 11/21 had detectable Th responses [Kaul1999]					
398	polyclonal	gp160 (300–322)	gp120 (IIIB)	CNNTRKSIRIQRGPGRAFVTIGK	L		guinea pig (IgG)
		Ab type V3 **Donor** D. Bolognesi and T. Matthews, Duke University **References** Allaway1993 • Synergy with combinations of CD4-based molecules in inhibition of HIV-1 Env mediated cell fusion [Allaway1993]					
399	polyclonal (VEI3)	gp160 (300–328)	Env	NNNTRKSIRIGPGRAFYTTGDIGNI-RQ		HIV-1 infection	human
		Ab type V3 **References** Carlos1999 • Antibody response to the epitopes in a vaccine construct (VEI) containing peptides from 5 hypervariable regions of gp120 was detected in the sera of HIV-1 positive subjects, including sera from 6 non-subtype B infections – serum samples from San Francisco, Canada and Puerto Rico cohort showed presence of antibodies against all five VEI hypervariable regions, but most consistently against the V3 region peptide NNNTRKSIRIGPGRAFYTTGDIGNIRQ [Carlos1999]					
400	9284 (NEA 9284)	gp160 (301–312)	gp120 (307–318 IIIB)	NNTRKSIRIQRG	L	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* inactivated virus *Strain:* IIIB *HIV component:* virus **Ab type** V3 **Donor** Dupont de Nemours, Les Ulis, France or Wilmington, Delaware **References** Skinner1988b, Skinner1988a, Sattentau1991, Wyatt1992, McKeating1992a, Sattentau1993, Moore1993c, Trujillo1993, Thali1993, VanCott1994, Thali1994, Cook1994, Okada1994, Sorensen1994, Sattentau1995b, VanCott1995, Fontenot1995, Moore1996, Poignard1996a, Cao1997b, Binley1997a, Parren1998a, Schonning1998 • 9284: IIIB type-specific binding and neutralization [Skinner1988b] • 9284: Two fold increase in binding to gp120 in the presence of bound sCD4 [Sattentau1991] • 9284: Single amino acid substitutions in the C4 region (427 W/V or W/S) or at the base of the V3 loop (298 R/G) can significantly increase binding and neutralization– position 427 is also important for CD4 binding and anti-CD4 binding site MAbs [Wyatt1992] • 9284: Increased binding in the presence of sCD4 [Sattentau1993] • 9284: Inhibits C4 region antibodies (G3-299, G3-519) which have conformational requirements [Moore1993c] • 9284: Peptide RIQRGPGRAFVTIGKIGNMRQA – Reacts with three human brain proteins of 35, 55, 110 kd – called NEA-9284 [Trujillo1993] • 9284: Does not bind MN gp120, just IIIB [VanCott1994] • 9284: gp41 mutation that confers resistance to neutralization by anti-CD4 binding site antibodies does not reduce neutralizing efficiency of this V3 region MAb [Thali1994] • 9284: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – this MAb can inhibit gp120 binding to GalCer in vitro [Cook1994] • 9284: Binding domain aa 301-310: TRKSIRIQRG – mutations in the V3 loop from basic residues can destroy virus infectivity and syncytium formation: R306T, R309T and R313G can also reduce binding of V3 MAbs with two different binding sites: 9284 and 0.5beta – called NEA9284 [Okada1994]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 9284: Did not neutralize infection of HIV/HTLV-I pseudotype [Sorensen1994] • 9284: Binds equally well to monomer and oligomer, rapid association and potent neutralization of lab strains – neutralizes cell-free virus Hx10 [Sattentau1995b] • 9284: Used to monitor HIV-1 Env expression in infected H9 cells, binds native and reduced gp120s similarly [VanCott1995] • 9284: Binds V3 loop – anti-C1 MAbs 133/290 and 135/9 enhance binding – reciprocal binding inhibition of other anti-V3 MAbs [Moore1996] • 9284: V3 MAbs 9284, BAT123, 110.5, and 110.I could each significantly increase gp120 dissociation from virus, mimicking sCD4, and expose the gp41 epitope for MAb 50-69, in contrast to anti-V2 MAbs [Poignard1996a] • 9284: Virus with the V1-V2 loop deleted was viable and more susceptible to neutralization by CD4i MAb 17b, and anti-V3 MAbs 1121, 9284, and 110.4, but not to and CD4BS MAb F105 or sCD4 [Cao1997b] • 9284: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren1998a] • 9284: In a study of the influence of the glycan at position 306 of the V3 loop on MAb recognition, 9284 was found to have an inaccessible epitope on the oligomeric form of Env and anti-V3 MAbs were found to neutralize an HIV-BRU mutant virus that lacks the V3 loop glycan more efficiently than HIV-BRU [Schonning1998]			
401	polyclonal	gp160 (301–325)	gp120 (IIIB)	NNTRKSIRIQRGPGRAFVTIGKIGN	L	Vaccine	murine (IgA)
		Vaccine *Vector/Type:* peptide *Strain:* IIIB *Adjuvant:* cholera toxin adjuvant **Ab type** V3 **References** Bukawa1995 • Polyclonal secretory IgA antibody raised by mucosal immunization is able to neutralize IIIB, SF2, and MN – HIV-1 neutralization may be due to V3, CD4 or HPG30 component of the multicomponent peptide immunogen [Bukawa1995]					
402	polyclonal	gp160 (301–325)	gp120 (IIIB)	NNTRKSIRIQRGPGRAFVTIGKIGN	L	Vaccine	murine (IgA22a)
		Vaccine *Vector/Type:* DNA *Strain:* IIIB *HIV component:* Env, Rev **Ab type** V3 **References** Sasaki1998 • An anti-env response was sought, and co-expression of Rev was required – intramuscular versus nasal vaccination with DNA vaccine with a QS21 adjuvant was studied – QS21 enhanced the IgG2a response mediated via Th1 cytokines IFNgamma and IL-2 [Sasaki1998]					
403	polyclonal	gp160 (302–317)	Env (B consensus)	NTRKSIHIGPGRAF		HIV-1 infection	human
		Ab type V3 **References** Morris2001 • Ab responses before HAART therapy and after one year of therapy were measured in 8 individuals that were classified HAART successes, and 10 patients who were classified as HAART failures – V3 peptide antibody binding titers to the B-consensus and MN and SF2 variants, and neutralization of HIV-1 MN and four subtype B clinical isolates were tested – subjects with strong anti-V3 and NAb humoral immune responses before starting HAART were more likely to achieve sustained viral suppression to <500 copies RNA/ml on HAART – HIV-specific Ab responses declined after 1 year of successful viral suppression on HAART [Morris2001]					
404	polyclonal	gp160 (302–318)	Env	NTRKSIHIGPGRAFY	L P	HIV-1 infection	human
		Ab type V3 **References** Bongertz2001					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• Non-transmitting mothers had an increased frequency of high neutralizing plasma Ab titers against HIV-1 MN (1:50 dilution, >90% neutralization, 33/88 pregnant women), compared to plasma from transmitting mothers (0/8 pregnant women) – non-transmitting mothers also had more potent neutralization against primary isolates from transmitting mothers, but neutralization of autologous virus was comparable for non-transmitting (7/13) and transmitting mothers (2/4) [Bongertz2001]					
405	MAG 109	gp160 (302–321)	gp120 (302–321 BH10)	NTRKSIRIQRGPGRAFVTIG	L	Vaccine	murine
		Vaccine *Vector/Type:* sCD4-gp120 complex *Strain:* HXB2 *HIV component:* gp120 **Ab type** V3 **References** Kang1994 • MAG 109: Binds a V3 loop peptide – sensitive to both V3 loop mutations and a mutation at the base of the V1/V2 loop structure (120/121 VK/LE) [Kang1994]					
406	MAG 49 (#49)	gp160 (302–321)	gp120 (302–321 BH10)	NTRKSIRIQRGPGRAFVTIG	L	Vaccine	murine
		Vaccine *Vector/Type:* sCD4-gp120 complex *Strain:* HXB2 *HIV component:* gp120 **Ab type** V3 **References** Kang1994, Moore1996 • MAG 49: Binds a V3 loop peptide – sensitive to both V3 loop mutations and a mutation at the base of the V1/V2 loop structure (120/121 VK/LE) [Kang1994] • MAG 49: Called #49 in this text. Binding enhanced by anti-C1 MAbs 133/290, 135/9, and by many anti-CD4 binding site MAbs – reciprocal enhancement of some anti-V2 MAbs – reciprocal binding inhibition of anti-V3 MAbs [Moore1996]					
407	MAG 53	gp160 (302–321)	gp120 (302–321 BH10)	NTRKSIRIQRGPGRAFVTIG	L	Vaccine	murine
		Vaccine *Vector/Type:* sCD4-gp120 complex *Strain:* HXB2 *HIV component:* gp120 **Ab type** V3 **References** Kang1994 • MAG 53: Binds a V3 loop peptide – sensitive to both V3 loop mutations and a mutation at the base of the V1/V2 loop structure (120/121 VK/LE) [Kang1994]					
408	MAG 56	gp160 (302–321)	gp120 (302–321)	NTRKSIRIQRGPGRAFVTIG	L	Vaccine	murine
		Vaccine *Vector/Type:* sCD4-gp120 complex *Strain:* HXB2 *HIV component:* gp120 **Ab type** V3 **References** Kang1994 • MAG 56: Binds a V3 loop peptide – sensitive to both V3 loop mutations and a mutation at the base of the V1/V2 loop structure (120/121 VK/LE) [Kang1994]					
409	1324-E (1324E)	gp160 (303–308)	Env (subtype CRF01)	TRTSVR	L	HIV-1 infection	human (IgG1κ)
		Ab type V3 **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center) **References** Gorny1998, Zolla-Pazner1999a, Zolla-Pazner1999b, Nyambi2000 • 1324-E: A human MAb was derived from an HIV-1 E clade infection from a US service man who had served in Thailand, selected with the consensus V3 peptide from clade E – cross-reactive with V3 peptides, and gp120 from E, C and A clades, as well as cells infected with a C-clade primary isolate, but not with B and D clade V3 peptides or rgp120 – neutralizes E clade virus adapted for growth in H9 cells, but not 5 primary E clade isolates, including the autologous isolate – kinetic parameters were measured, 1324E was comparable to 447-52D [Gorny1998]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 1324-E: E clade stimulated MAb did not cross-react with B clade peptides nor did B clade derived peptides with an E clade V3 loop, but both E and B clade stimulated Abs can cross-react with some peptides from other clades – this Ab showed strong binding to several E, A and F peptides, one C peptide, and no reactivity with B peptides and most D peptides [Zolla-Pazner1999a] • 1324-E: MAb reacted with peptides from E clade, while B clade derived MAbs could not [Zolla-Pazner1999b] • 1324-E: Called 1324E – A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 1324E showed poor cross-reactivity, and was the only MAb tested that was derived from a non-B clade infected patient, an E clade infection was the source of 1324E [Nyambi2000]				
410	polyclonal	gp160 (303–319)	gp120 (subtype C)	CKRKIHIGPGQAFYT		Vaccine	murine (IgG2a, IgG2b)
		Vaccine *Vector/Type:* peptide in ISCOM or liposome *HIV component:* V3 *Adjuvant:* ISCOM **Ab type** V3 **References** Ahluwalia1997 • A V3 loop peptide modified to resemble an Indian form (GPGQ) was incorporated into ISCOMS (immune stimulating complexes) or liposomes, and used to immunize mice – the IgG2a/IgG2b antibody response was enhanced by the presentation in the ISCOM suggestive of a Th1 response [Ahluwalia1997]					
411	MO99/V3	gp160 (304–308)	gp120 (304–308 IIIB)	RKSIR	no	in vitro stimulation	human (IgM)
		Ab type V3 **References** Ohlin1992 • MO99: Generated through in vitro stimulation of uninfected-donor lymphocytes with rpB1 (IIIB Env 286-467) [Ohlin1992]					
412	C311E	gp160 (304–313)	gp120 (309–316 MN)	RKRIHIGP	L	HIV-1 infection	chimpanzee (IgG1)
		Ab type V3 **References** Warrier1996, Alsmadi1998 • C311E: Chimps were infected with HIV-1 IIIB, and this resulting MAb gave synergistic neutralization of HIV-1 when combined with anti-V2 MAb C108G [Warrier1996] • C311E: A study of 6 anti-Env MAbs and their ability to bind or direct ADCC against target cells infected with IIIB, MN, SF-2, and RF – C311E bound and directed lysis against all four strains [Alsmadi1998]					
413	907	gp160 (304–314)	gp120 (309–318)	RKSIRIQRGPG	L	Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* gp160 **References** Chesebro1988, Pincus1989, Pincus1991, Pincus1996 • 907: Strain specific binding, and neutralization of only the LAV strain [Chesebro1988] • 907: Coupled to ricin A chain (RAC), MAb 907 inhibited protein synthesis and cell growth in HIV-infected cells [Pincus1989] • 907: Epitope sequence is based on database count of a specified location – 924-RAC immunotoxin is IIIB strain-specific [Pincus1991] • 907: A panel of immunotoxins were generated by linking Env MAbs to ricin A – immunotoxins mediated cell killing, but killing was not directly proportional to binding [Pincus1996]					
414	924	gp160 (304–314)	gp120 (309–318 IIIB)	RKSIRIQRGPG		Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* gp160 **Ab type** V3 **References** Chesebro1988, Pincus1991, Pincus1993a, Pincus1993b, Cook1994, Pincus1996, Pincus1998 • 924: HIV IIIB strain specific [Chesebro1988]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 924: Epitope sequence is based on database count of a specified location – 924-RAC immunotoxin is IIIB strain-specific [Pincus1991] • 924: MAb was coupled to ricin A chain (RAC) – immunotoxin efficacy was not significantly decreased by sCD4, although the efficacy of gp41 MAb immunotoxins in vitro increased 30-fold by sCD4 [Pincus1993a] • 924: Ab response in IIIB lab workers was compared to gp160 LAI vaccine recipients – MAb 924 was used as a control – infected lab workers and a vaccinia gp160 vaccine had strong V3 MAb response, but alum absorbed rec gp160 did not generate anti-V3 response [Pincus1993b] • 924: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – this MAb can inhibit gp120 binding to GalCer in vitro [Cook1994] • 924: A panel of immunotoxins were generated by linking Env MAbs to ricin A – immunotoxins mediated cell killing, but killing was not directly proportional to binding [Pincus1996]					
415	polyclonal	gp160 (304–318)	gp120 (304–318 LAI)	RKSIRIQRGPGRAFV		in vitro stimulation	human (IgG, IgM)
		Ab type V3 **References** Chin1995 • Mimicking the humoral immune response in vitro supports isotype switching – human IgG MAbs were generated from naive donors [Chin1995]					
416	polyclonal	gp160 (304–318)	gp120 (304–318 LAI)	RKSIRIQRGPGRAFV		Vaccine	human (IgG, IgM)
		Vaccine *Vector/Type:* peptide *Strain:* LAI **Ab type** V3 **References** Zafiropoulos1997 • IgG to IgM isotype switching in response to primary and secondary peptide vaccinations was studied – the immunogen contained a V3 loop fragment and a tetanus toxin helper epitope [Zafiropoulos1997]					
417	10F10	gp160 (304–320)	gp120 (MN)	RKRIHIGPGRAFYTT	L	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* peptide *Strain:* MN *HIV component:* gp120 **Ab type** V3 **References** Duarte1994 • 2C4: Putative epitope lies within IHIGPGRAFYT – generated by multi-epitope polypeptide immunization – recognize MN and SC (TRSIHIGPGRAFYTT) peptides, lower affinity for SF2 [Duarte1994]					
418	2C4	gp160 (304–320)	gp120 (MN)	RKRIHIGPGRAFYTT	L (MN)	Vaccine	murine (IgG2a)
		Vaccine *Vector/Type:* peptide *Strain:* MN **Ab type** V3 **References** Duarte1994 • 2C4: Putative epitope lies within IHIGPGRAFYT – neutralizes MN, not IIIB and SF2 – generated by multi-epitope polypeptide immunization – recognize MN and SC (TRSIHIGPGRAFYTT) peptides, lower affinity for SF2 [Duarte1994]					
419	412-D (412-10D, 412, 412D)	gp160 (304–320)	gp120 (MN)	RKRIHIGPGRAFYTT	L	HIV-1 infection	human (IgG1κ)
		Ab type V3 **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center) **References** Gorny1993, Spear1993, VanCott1994, Fontenot1995, Gorny1998, Nyambi1998, Zolla-Pazner1999a, Zolla-Pazner1999b, Nyambi2000 • 412-D: Neutralizes MN, does not bind SF2 or HXB2 – not reactive with hexa or heptapeptides by Pepscan [Gorny1993] • 412-D: Mediated deposition of complement component C3 on HIV infected cells, enhanced by second Ab binding, rabbit anti-human IgG [Spear1993] • 412-D: Called 412-10D – relatively rapid dissociation and weak homologous neutralization [VanCott1994] • 412-D: Called 412 – The tip of the V3 loop was presented in a mucin backbone – higher valency correlates with stronger affinity constant [Fontenot1995]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 412-D: Kinetic parameters were measured, and the association rates were similar, but dissociation rate constants were quite variable for V3 MAbs, 412-D has a relatively fast dissociation, thus low affinity among V3 MAbs [Gorny1998] • 412-D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – 412-D was bound only to B clade virions and to D clade MAL [Nyambi1998] • 412-D: Review of clade specificity and anti-V3 HIV-1-Abs [Zolla-Pazner1999a] • 412-D: MAb peptide-reactivity pattern clustered with immunological related MAbs: 391.5, 412 and 418, all selected with MN V3 peptide – the core amino acids HIGPGR tended to be critical for reactivity in this group [Zolla-Pazner1999b] • 412-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 412-D showed limited reactivity [Nyambi2000]				
420	polyclonal	gp160 (304–320)	gp120 (MN)	RKRIHIGPGRAFYTT	L (MN ALA-1)	HIV-1 infection	human
		Ab type V3 **References** Spear1994 • 40% of antibody in serum that can bind to native viral proteins on MN-infected cells can be blocked by the peptide RKRIHIGPGRAFYTT, which can also block 75-95% of the complement activation on HIV infected cells [Spear1994]					
421	CGP 47 439	gp160 (304–322)	gp120	RKRIRIQRGPGRAFVTIGK?	L	Vaccine	human (Ig)
		Vaccine *Vector/Type:* protein *Strain:* IIIB *HIV component:* gp120 **Ab type** V3 **References** Liou1989, Safrit1993, Gunthard1994, Gauduin1998, Jacobson1998 • CGP 47 439: passive transfer to Hu-PBS-SCID mice confers protection against challenge with homologous cell-free virus – CGP 47 439 is a BAT123-human Ig chimera [Safrit1993] • CGP 47 439: Phase I/IIA clinical trial studying multidose tolerability, immunogenicity and pharmacokinetic responses – GP 47 439 was well tolerated, serum t_1/2 was 8-16 days, and a virus burden reduction was noted in some patients [Gunthard1994] • CGP 47 439: Post-exposure passive transfer of murine BAT123 can confer protection to hu-PBL-SCID mice challenged with HIV-1 LAI – this protection is not elicited by CGP 47 439, suggesting that the protection is mediated by complement – the protective ability of BAT123 is lost when mice were treated with cobra venom factor, which inactivates serum complement – in this circumstance complement activation provided a protective advantage [Gauduin1998] • CGP 47 439: Review of passive immunotherapy, summarizing [Gunthard1994] in relation to other studies [Jacobson1998]				
422	polyclonal	gp160 (304–322)	(MN)	RKRIHIGPGRAFYTTKN		HIV-1 infection	human
		Ab type V3 **References** Cheingsong-Popov1992 • The Ab response of 829 HIV-1 infected subjects from eight geographic areas to a set of different V3 peptides was determined by ELISA and cross-inhibition studies – the Ab binding pattern was highly variable, depended on the geographic origin of the sample – 297 sera were tested in a neutralization assay – there was a correlation between Ab binding to the MN V3 loop and MN neutralizing titer, but with neutralization of IIIB or CBL-4 [Cheingsong-Popov1992]					
423	178.1 (178.1.1)	gp160 (305–309)	gp120 (305–309 BH10)	KSiRI	L	Vaccine	murine (IgG2a)
		Vaccine *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* yeast derived gp160 **Ab type** V3 **Donor** C. Thiriart, Smith Kline and MRC AIDS reagent project **References** Thiriart1989, Back1993, Moore1993a, Cook1994 • 178.1: Reacts to gp120 and gp160 in RIPA EIA and immunoblot [Thiriart1989] • 178.1: Called 178.1.1 – conformational, does not bind well to denatured gp120 [Moore1993a]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 178.1: gp41 amino acid substitutions 668 (N/S) and 675 (I/M) in gp41 interfere with 5023s neutralization potency, region 662-675 is ELDKWANLWNWFNI [Back1993]
- 178.1: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – this MAb can inhibit gp120 binding to GalCer in vitro – binding of GalCer to gp120 inhibited but did not completely block MAb binding[Cook1994]
- 178.1: UK Medical Research Council AIDS reagent: ARP331

424 257-D (257, 257-2-D-IV, 257-D-IV, 257, 257-2D, 257D, ARP3023) gp160 (305–309) gp120 (MN) KRIHI L HIV-1 infection human (IgG1λ)

Ab type V3 **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)

References Gorny1991, D'Souza1991, Karwowska1992b, Gorny1993, Cavacini1993a, Spear1993, D'Souza1994, VanCott1994, Stamatatos1995, D'Souza1995, Zolla-Pazner1995a, Schutten1995a, Schutten1995b, Fontenot1995, Wisnewski1996, Schutten1996, Schutten1997, Stamatatos1997, Hill1997, Hioe1997b, LaCasse1998, Yang1998, Gorny1998, Stamatatos1998, Zolla-Pazner1999a, Zolla-Pazner1999b, Beddows1999, Oggioni1999, Nyambi2000, Park2000, York2001, Zhang2002

- 257-D: Called 257-2-D-IV – potent neutralizing MAb [D'Souza1991]
- 257-D: Reacts with MN, NY5, CDC4 and SF2, does not cross-react with RF, WM52, or HXB2 [Karwowska1992b]
- 257-D: Neutralizes MN – binds SF2: KSIYI – specificity: MN, SF2, NY5, RF. [Gorny1993]
- 257-D: Additive MN or SF2 neutralization when combined with CD4 binding site MAb F105 – does not neutralize RF [Cavacini1993a]
- 257-D: Mediated deposition of complement component C3 on HIV infected cells, enhanced by second Ab binding, rabbit anti-human IgG – complement mediated virolysis of MN, but not in the presence of sCD4 [Spear1993]
- 257-D: Included a multi-lab study for antibody characterization and assay comparison – best NAb against MN, but not IIIB [D'Souza1994]
- 257-D: Potent MN neutralization, slow dissociation constant [VanCott1994]
- 257-D: The binding of conformation-dependent anti-V2, anti-V3, and anti-CD4BS MAbs to monomeric and virion-associated gp120 from HIV-1 isolates with differences in cell tropism was studied – V3 loop epitopes were less accessible to Ab binding on the virion surface than in the gp120 monomer, particularly for macrophage-tropic isolates SF162 and SF128a, relative to T-cell tropic SF2 – sCD4 association with gp120 better revealed this V3 epitope on TCLA SF2 and dual tropic (MU3) viruses than on macrophage tropic isolates [Stamatatos1995]
- 257-D: Called 257-D-IV – could neutralize MN and closely related JRCSF, but not 2 B subtype and 1 D subtype primary isolates in a multi-laboratory study involving 11 labs [D'Souza1995]
- 257-D: In serotyping study using flow-cytometry, bound only to virus with KRIHI [Zolla-Pazner1995a]
- 257-D: Only inhibition of SI phenotype virus, and strong enhancement of NSI phenotype chimeric viruses, that incorporated different envs from the same donor [Schutten1995a]
- 257-D: Comparable affinity for SI and NSI viruses, in contrast to MAb MN215 [Schutten1995b]
- 257-D: 257-D is V H5 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals [Wisnewski1996]
- 257-D: IIIB neutralizing MAbs in vitro fail to neutralize in a mouse model it in vivo [Schutten1996]
- 257-D: Neutralized (>90%) an SI-env chimeric virus and enhanced (>200%) an NSI-env chimeric virus [Schutten1997]
- 257-D: Binds less extensively than MAb 391-95D on the surface of HIV-1 isolates SF162 and SF128A – neutralizes less potently than 391-95D – stronger neutralization of primary macrophage targets than PBMC [Stamatatos1997]
- 257-D: Called 257 – gp120 can inhibit MIP-1alpha from binding to CCR5, but this inhibitory effect is blocked by pre-incubation of gp120 with three anti-V3 MAbs: 447, 257, 1027 – MAb 670 which binds in the C5 region had no effect [Hill1997]
- 257-D: A T-cell line-adapted (TCLA) derivative of SI primary isolate 168P acquired the ability to be neutralized by anti-V3 MAbs – the primary isolate could use either CCR5 or CXCR4, and was not neutralized when infection was directed via either pathway, however the TCLA derivative uses CXCR4 only and is neutralized [LaCasse1998]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 257-D: A neutralization assay was developed based on hemi-nested PCR amplification of the LTR (HNPCR) – LTR-HNPCR consistently revealed HIV DNA and was shown to be a rapid, specific and reliable neutralization assay based on tests with 6 MAbs and 5 isolates [Yang1998]
- 257-D: Kinetic parameters were measured, and the association rates were similar, but dissociation rate constants were quite variable for V3 MAbs, 257-D has a slow dissociation, thus the highest affinity among V3 MAbs [Gorny1998]
- 257-D: Called 257D – deleting the V2 loop of neutralization-resistant HIV-1 isolate SF162 does not abrogate its replication in PBMC or macrophages, but it enhances its neutralization sensitivity to sera from patients with B clade infection up to 170-fold, and also enhances sensitivity to sera from clades A through F – deletion of V1 or V2 did not enable neutralization by V3 MAbs 391-95D or 257D [Stamatatos1998]
- 257-D: Review of clade specificity and anti-V3 HIV-1-Abs [Zolla-Pazner1999a]
- 257-D: MAb peptide reactivity pattern clustered with immunological related MAbs: 1108, 386, 268, 311, 257, 694.8 – the amino acids HI tended to be critical for reactivity in this group [Zolla-Pazner1999b]
- 257-D: rgp120 derived from a R5X4 subtype B virus, HIV-1 W61D, was used to vaccinate healthy volunteers and the resulting sera were compared with sera from HIV-1 positive subjects and neutralizing MAbs – 257-D bound rgp120 W61D but could only neutralize the W61D isolate following T-cell line adaptation [Beddows1999]
- 257-D: Study of a live-vector mucosal vaccine that expresses HIV-1 V3 domains using the bacterium Streptococcus gordonii which can express heterologous Ag and can colonize the oral cavity and vagina of mice – 268-D and 257-D recognized S. gordonii expressing the V3 domain of MN – the vaccine stimulated V3-specific IgG2a in mice [Oggioni1999]
- 257-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 257-D showed intermediate reactivity [Nyambi2000]
- 257-D: Called 257D – six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20-100 fold more efficient at neutralizing the sensitive form – the mutation L544P reduced binding of all MAbs against gp120 by causing conformational changes [Park2000]
- 257-D: Abs against the V3 loop (50.1, 58.2, 59.1, 257-D, 268-D, 447-52D), CD4BS (IgG1b12, 559-64D, F105), CD4i (17b), and to gp41 (2F5, F240) each showed similar binding efficiency to Env derived from related pairs of primary and TCLA lines (primary: 168P and 320SI, and TCLA: 168C and 320SI-C3.3), but the TCLA lines were much more susceptible to neutralization suggesting that the change in TCLA lines that make them more susceptible to NAbs alters some step after binding [York2001]
- 257-D: Called ARP3023: Herpesvirus saimiri-immortalized CD4+ T lymphocytes (HVS T cells) were used to isolate virus and perform HIV-1 neutralization assays, and compared with a standard PBMC protocol – neutralization sensitivities to a panel of MAbs and to homologous or heterologous plasma/sera were similar for HVS T cells (CN-2 cells) and PBMCs [Vella2002]
- 257-D: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain [Zhang2002]
- 257-D: UK Medical Research Council AIDS reagent: ARP3023
- 257-D: NIH AIDS Research and Reference Reagent Program: 1510

425	311-11-D (311-11D, 311, 311D, 311-D)	gp160 (305–313)	gp120	KRIHIGP	L	HIV-1 infection	human (IgG1λ)

Ab type V3 **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny1991, Gorny1993, Spear1993, Gorny1998, Zolla-Pazner1999a, Zolla-Pazner1999b, Nyambi2000

- 311-11-D: Neutralizes MN – binds SF2: KSIYIGP [Gorny1993]
- 311-11-D: Mediated deposition of complement component C3 on HIV infected cells, enhanced by second Ab binding, rabbit anti-human IgG [Spear1993]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 311-11-D: Review of clade specificity and anti-V3 HIV-1-Abs [Zolla-Pazner1999a] • 311-11-D: MAb peptide reactivity pattern clustered with immunological related MAbs: 1108, 386, 268, 311, 257, 694.8 – the amino acids HI tended to be critical for reactivity in this group [Zolla-Pazner1999b] • 311-11-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 311-11D showed weak reactivity [Nyambi2000]					
426	41148D	gp160 (305–313)	gp120 (MN)	KRIHIGP	L	HIV-1 infection	human (IgG1)
		Ab type V3 **References** Pinter1993b, Alsmadi1998 • 41148D: Neutralizes less potently than 4117C, reacts with MN, IIIB, SF2 [Pinter1993b] • 41148D: A study of 6 anti-Env MAbs and their ability to bind or direct ADCC against target cells infected with IIIB, MN, SF-2, and RF – bound and directed lysis against strains IIIB, MN, SF-2, comparable to 4117C, however 41148D is 10x less efficient at neutralization, showing ADCC and neutralization don't always correlate [Alsmadi1998]					
427	391/95-D (391-95D, 391.5, 391/95D)	gp160 (305–318)	gp120 (MN)	KRIHIGPGRAFY	L	HIV-1 infection	human (IgG1κ)
		Ab type V3 **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center) **References** Gorny1991, Gorny1993, Fontenot1995, Stamatatos1995, Seligman1996, Stamatatos1997, Stamatatos1998, Zolla-Pazner1999a, Zolla-Pazner1999b, Ly2000, Park2000, Guillon2002, Lawson2002, Zhang2002 • 391/95-D: Neutralizes MN – binds to SF2, not IIIB [Gorny1993] • 391/95-D: The binding of conformation-dependent anti-V2, anti-V3, and anti-CD4BS MAbs to monomeric and virion-associated gp120 from HIV-1 isolates with differences in cell tropism was studied – V3 loop epitopes were less accessible to Ab binding on the virion surface than in the gp120 monomer, particularly for macrophage-tropic isolates SF162 and SF128a, relative to T-cell tropic SF2 – sCD4 association with gp120 better revealed this V3 epitope on macrophage tropic and dual tropic (MU3) viruses, but not in TCLA SF2 [Stamatatos1995] • 391/95-D: Competition ELISAs with serial deletions estimated the epitope to be KRIHIGPGRAFY – unconstrained peptide had higher affinity than cyclic [Seligman1996] • 391/95-D: Called 391-95D – binds more extensively than MAb 257-D on the surface of HIV-1 isolates SF162 and SF128A – neutralizes more potently than 257-D – stronger neutralization of primary macrophage targets than PBMC – binding post-gp120-sCD4 association related to anti-V3 Abs neutralizing capacity [Stamatatos1997] • 391/95-D: Called 391-95D – deleting the V2 loop of neutralization-resistant HIV-1 isolate SF162 does not abrogate its replication in PBMC or macrophages, but it enhances its neutralization sensitivity to sera from patients with B clade infection up to 170-fold, and also enhances sensitivity to sera from clades A through F – deletion of V1 or V2 did not enable neutralization by V3 MAbs 391-95D or 257D [Stamatatos1998] • 391/95-D: Review of clade specificity and anti-V3 HIV-1-Abs [Zolla-Pazner1999a] • 391/95-D: Called 391.5 – MAb peptide-reactivity pattern clustered with immunological related MAbs: 391.5, 412 and 418, all selected with MN V3 peptide – the core amino acids HIGPGR tended to be critical for reactivity in this group [Zolla-Pazner1999b] • 391/95-D: Called 391-95D – SF162 is a neutralization-resistant HIV-1 isolate – N-linked glycosylation modifications in the V2 loop of the SF162 gp120 revealed that these sites prevent neutralization by CD4BS MAbs (IgG1b12 and IgGCD4), and protect against neutralization by V3 MAbs (447-D and 391-95D) – V2-region glycosylation site mutations did not alter neutralization resistance to V2 MAbs (G3.4 and G3.136) or CD4i MAbs (17b and 48d) – V2 glycosylation site modification allows infection of macrophages, probably due to glycosylated forms requiring fewer CCR5 molecules for viral entry [Ly2000] • 391/95-D: Called 391/95D – six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20-100 fold more efficient at neutralizing the sensitive form – the mutation L544P reduced binding of all MAbs against gp120 by causing conformational changes [Park2000]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 391/95-D: The affect of Ab binding on infectivity was studied by pseudotyping three related envs with different phenotypes – R5 viruses were preferentially enhanced, not X4 – the V3 region was the main determinant of Ab-mediated enhancement and modulation of the interaction between CCR5 and gp120 is critical – tests with MAbs anti-V3 391/95-D and CD4BS-specific GP68 indicate that Ab specificity did not determine whether or not infectivity was enhanced or neutralized, rather the phenotype was determined by Env conformation [Guillon2002] • 391/95-D: The phenotype and genotype of viral env sequences were studied over a period of seroconversion in one individual – Env trans-complementation demonstrated infectivity of clones derived pre-seroconversion were not influenced by MAb 391/95-D, but post-seroconversion clones were enhanced in the presence of 391/95-D, although the V3 binding region was unchanged – a change in the CD4-binding site was observed (NL43 427 Glu–>Lys) to be present in the post-seroconversion 391/95-D enhanced clone (see [Guillon2002]) [Lawson2002] • 391/95-D: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain [Zhang2002]			
428	Aw	gp160 (305–320)	gp120 (Gun-1wt)	KSITIGPGRAFHAI	L	Vaccine	rat
		Vaccine *Vector/Type:* peptide *Strain:* Gun-1 *HIV component:* V3 **Ab type** V3 **References** McKnight1995 • Aw: Rat antibodies were raised against V3 peptides that represent either the wildtype (wt), or brain-cell tropic variant (v) of the isolate Gun-1 – Aw gives weak neutralization of both wildtype and v strains [McKnight1995]					
429	Bw	gp160 (305–320)	gp120 (Gun-1wt)	KSITIGPGRAFHAI	L	Vaccine	rat
		Vaccine *Vector/Type:* peptide *Strain:* Gun-1 *HIV component:* V3 **Ab type** V3 **References** McKnight1995 • Bw: Rat antibodies were raised against V3 peptides that represent either the wildtype (wt), or brain-cell tropic variant (v) of the isolate Gun-1 – Bw gives weak neutralization of only the wildtype strain, does not bind to variant [McKnight1995]					
430	DO142-10 (DO 142-10)	gp160 (305–320)	gp120 (MN)	KRIHIGPGRAFYTT	L	HIV-1 infection	human Fab (IgG1)
		Ab type V3 **References** Seligman1996, Ditzel1997, Parren1997c, Parren1997a, Parren1998a, Sullivan1998a • DO142-10: Fab fragment – competition ELISAs with serial deletions defined the epitope KRIHIGPGRAFYTT [Seligman1996] • DO142-10: Phage expression libraries panned against MN peptide were used to select Fab DO142-10 – Fab binds MN gp120, but not a primary isolate rec gp120 [Ditzel1997] • DO142-10: Neutralizes TCLA strains but not primary isolates [Parren1997c] • DO142-10: Binds to gp120 MN and an MN V3 peptide with equal affinity, but binds a consensus B peptide and JRCSF less well, and to IIIB gp120 not at all [Parren1997a] • DO142-10: The rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142-10 > DA48 > L17) was markedly different that Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142-10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren1998a]			

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• DO124-10: The HIV-1 virus YU2 entry can be enhanced by MAbs binding to the CD4BS, V3 loop, and CD4i epitopes – the activation for this enhanced entry state could be conferred on HxB2 by introducing the YU2 V3 loop, or the YU2 V3 and V1/V2 loops – a similar effect is observed by sub-neutralizing concentrations of sCD4 and the effect is dependent of CCR5 – Fab Ab fragment DO124-10 also enhances YU2 entry, ruling out Fc interactions or Env cross-linking as a mechanism – while DO124-10 enhances YU2 entry 6-fold, it neutralizes HXBc2 under identical conditions [Sullivan1998a]					
431	Dv	gp160 (305–320)	gp120 (Gun-1v)	KSITIGSGRAFHAI	L	Vaccine	rat
		Vaccine *Vector/Type:* peptide *Strain:* Gun-1 *HIV component:* V3 **Ab type** V3 **References** McKnight1995 • Dv: Rat antibodies were raised against V3 peptides that represent either the wildtype (wt), or brain-cell tropic variant (v) of the isolate Gun-1 – neutralization of only the variant strain, does not bind to wildtype [McKnight1995]					
432	Fv	gp160 (305–320)	gp120 (Gun-1v)	KSITIGSGRAFHAI	L	Vaccine	rat
		Vaccine *Vector/Type:* peptide *Strain:* Gun-1 *HIV component:* V3 **Ab type** V3 **References** McKnight1995 • Fv: Rat antibodies were raised against V3 peptides that represent either the wildtype (wt), or brain-cell tropic variant (v) of the isolate Gun-1 – neutralization of only the variant strain, does not bind to wildtype [McKnight1995]					
433	Gv	gp160 (305–320)	gp120 (Gun-1v)	KSITIGSGRAFHAI	L	Vaccine	rat
		Vaccine *Vector/Type:* peptide *Strain:* Gun-1 *HIV component:* V3 **Ab type** V3 **References** McKnight1995 • Gv: Rat antibodies were raised against V3 peptides that represent either the wildtype (wt), or brain-cell tropic variant (v) of the isolate Gun-1 – neutralization of only the variant strain, does not bind to wildtype [McKnight1995]					
434	Hv	gp160 (305–320)	gp120 (Gun-1v)	KSITIGSGRAFHAI	L	Vaccine	rat
		Vaccine *Vector/Type:* peptide *Strain:* Gun-1 *HIV component:* V3 **Ab type** V3 **References** McKnight1995 • Hv: Rat antibodies were raised against V3 peptides that represent either the wildtype (wt), or brain-cell tropic variant (v) of the isolate Gun-1 – neutralization of only the variant strain, does not bind to wildtype [McKnight1995]					
435	polyclonal	gp160 (305–322)	gp140 (SF162)	KSITIGPGRAFYATGD	yes	Vaccine	rabbit, Rhesus macaque (IgG)
		Vaccine *Vector/Type:* DNA with CMV promotor *Strain:* SF162, SF162DeltaV2 *HIV component:* gp140 *Adjuvant:* MF-59C **Ab type** V3 **References** Barnett2001 • SF162DeltaV2 is a virus that has a 30 amino acids deletion in the V2 loop that does not abrogate its infectivity but renders it highly susceptible to neutralization – when incorporated into a codon-optimized DNA vaccine with a CMV promoter, delivered by gene gun, SF162DeltaV2 gave higher neutralizing Ab titers against SF162 than did SF162 itself, and Abs that cross-neutralized non-homologous primary isolates were obtained only when SF162DeltaV2, but not intact SF162, was used as the immunogen – NAbs titers specific for SF162 increased with multiple immunizations, while titers for non-homologous isolates decreased, but anti-V3 peptide binding Abs were not likely the source of this distinction because anti-V3 titers were much lower than those against the entire envelope, and the second booster immunization did not increase the titer of anti-V3 loop Abs [Barnett2001]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
436	50.1 (R/V3-50.1, Fab 50.1)	gp160 (306–310)	gp120 (MN)	RIHIG	L	Vaccine	murine (IgG1κ)

Vaccine *Vector/Type:* peptide *Strain:* MN *HIV component:* V3
Ab type V3 **Donor** Mary White-Scharf, Repligen Corporation, Cambridge, MA
References D'Souza1991, White-Scharf1993, Potts1993, Ghiara1993, Rini1993, Bou-Habib1994, VanCott1994, Robert-Guroff1994, Moore1994b, VanCott1995, Fontenot1995, Seligman1996, Berman1997, LaCasse1998, Stanfield1999, Hoffman1999, Park2000, York2001, Zhang2002

- 50.1: Called R/V3-50.1 – potent neutralizing of lab strains[D'Souza1991]
- 50.1: Epitope defined by peptide reactivity and changes affinity with amino acid substitutions – epitope RIHIGP [White-Scharf1993]
- 50.1: No synergistic neutralization of MN when combined with CD4BS MAb F105 – isotype stated to be IgG2a [Potts1993]
- 50.1: Crystal structure of a 24 amino acid peptide from the V3 loop bound to 59.1 and 50.1 Fab fragments – epitope KRIHIGP [Ghiara1993]
- 50.1: Crystal structure of V3 loop bound to 50.1 – light chain binds just to the left of GPG, heavy chain binds further to the left [Rini1993]
- 50.1: No neutralization of primary isolate JR-CSF – greater affinity for and neutralization of T cell tropic strain T-CSF, derived from JR-CSF [Bou-Habib1994]
- 50.1: Potent MN neutralization, slow dissociation rate [VanCott1994]
- 50.1: Chimeric MN V3 loop in an HXB2 background allows increased FACS signal, Ab affinity, and viral neutralization [Robert-Guroff1994]
- 50.1: Shows modest cross-reactivity among B clade gp120s, little outside B clade [Moore1994b]
- 50.1: Used to monitor HIV-1 Env expression in infected H9 cells [VanCott1995]
- 50.1: Competition ELISAs with serial deletions produced comparable estimate of epitope length to crystal structure and alanine substitution – KRIHIGP [Seligman1996]
- 50.1: Binds to 6/7 isolates from breakthrough cases from a MN gp120 vaccine trial [Berman1997]
- 50.1: A T-cell line-adapted (TCLA) derivative of SI primary isolate 168P acquired the ability to be neutralized by anti-V3 MAbs – the primary isolate could use either CCR5 or CXCR4, and was not neutralized when infection was directed via either pathway, however the TCLA derivative uses CXCR4 only and is neutralized [LaCasse1998]
- 50.1: The crystal structure of V3 loop peptides bound to Fabs was obtained – conformational changes in the tip of the V3 loop (GPGR) were observed when different Fabs were bound [Stanfield1999]
- 50.1: Called R/V3-50.1 – six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20-100 fold more efficient at neutralizing the sensitive form – the mutation L544P reduced binding of all MAbs against gp120 by causing conformational changes – 50.1 could only neutralize the sensitive form [Park2000]
- 50.1: Abs against the V3 loop (50.1, 58.2, 59.1, 257-D, 268-D, 447-52D), CD4BS (IgG1b12, 559-64D, F105), CD4i (17b), and to gp41 (2F5, F240) each showed similar binding efficiency to Env derived from related pairs of primary and TCLA lines (primary: 168P and 320SI, and TCLA: 168C and 320SI-C3.3), but the TCLA lines were much more susceptible to neutralization suggesting that the change in TCLA lines that make them more susceptible to NAbs alters some step after binding – the dissociation constant, Kd of 50.1 for the cell associated primary and TCLA Envs was equal, 7nM [York2001]
- 50.1: Called R/V3-50.1 – A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain [Zhang2002]
- 50.1: NIH AIDS Research and Reference Reagent Program: 1289

437	polyclonal	gp160 (306–318)	gp120 (NY5)	KKGIAIGPGRTLY			(IgM)

Ab type V3
References Metlas1999b, Metlas1999a

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• Auto-Abs that react with the V3 loop of NY5 are present in the sera of HIV- individuals, and are predominantly IgM [Metlas1999b]					
438	BAT123 (BAT-123, CGP 47 439)	gp160 (306–322)	gp120 (308–322 HXB2)	RIRIQRGPGRAFVTIGK	L	Vaccine	murine (IgG1κ)

Vaccine *Vector/Type:* inactivated virus *Strain:* IIIB *HIV component:* virus
Ab type V3 **Donor** Tanox Biosystems Inc and David Ho, ADARC, NY
References Fung1987, Liou1989, Fung1990, Moore1993a, Safrit1993, Thali1993, Pirofski1993, Gauduin1995, Sattentau1995b, Poignard1996a, Andrus1998, Parren1998a, Gauduin1998

- BAT123: CGP 47 439 is a BAT123 chimera that has a human IgG1 Fc domain
- BAT123: Anti-idiotypic MAb, AB19-4i, stimulates anti-anti-ID which neutralizes MN and IIIB [Fung1990]
- BAT123: Called BAT-123 – conformational, does not bind well to denatured gp120 – not reactive with SF-2 gp120 – does not inhibit HIV-1 sera from binding to IIIB gp120 [Moore1993a]
- BAT123: Passive transfer to Hu-PBS-SCID mice confers protection against challenge with homologous cell-free virus [Safrit1993]
- BAT123: Variable region sequenced – heavy chain: V 3660-SB32, D unknown, J H3 – light chain: V kappa21, J kappa2 [Pirofski1993]
- BAT123: Passive transfer of BAT123 to hu-PBL-SCID mice 1 hour prior to inoculation with HIV-1 LAI, or up to four hours post-exposure, could protect mice from infection – the protection, like the MAb, was specific for the viral strain LAI [Gauduin1995]
- BAT123: Binds with high affinity to monomer and oligomer, rapid association and potent neutralization of lab strain [Sattentau1995b]
- BAT123: Epitope described as RGPGRAFVTIGK – V3 MAbs 9284, BAT123, 110.5, and 110.I could each significantly increase gp120 dissociation from virus (BAT123 less so than the others), mimicking sCD4, and expose the gp41 epitope for MAb 50-69, in contrast to anti-V2 MAbs [Poignard1996a]
- BAT123: Post-exposure prophylaxis was effective when MAb 694/98-D was delivered 15 min post-exposure to HIV-1 LAI in hu-PBL-SCID mice, but declined to 50% if delivered 60 min post-exposure, and similar time constraints have been observed for HIVIG, 2F5 and 2G12, in contrast to MAb BAT123 that could protect delivered 4 hours post infection [Andrus1998]
- BAT123: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren1998a]
- BAT123: Post-exposure passive transfer of murine BAT123 can confer protection to hu-PBL-SCID mice challenged with HIV-1 LAI – this protection is not elicited by CGP 47 439, a BAT123 chimera that has a human IgG1 Fc domain, suggesting that the protection is mediated by complement – the protective ability of BAT123 is lost when mice were treated with cobra venom factor, which inactivates serum complement – IgG1 does not fix complement efficiently so an IgG2 MAb might perform better [Gauduin1998]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
439	838-D (838)	gp160 (307–311)	Env (RF)	KSITK	L	HIV-1 infection	human (IgG1λ)

Ab type V3 **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny1997, Hioe1997b, Nyambi1998, Zolla-Pazner1999a, Zolla-Pazner1999b, Gorny2000a, Nyambi2000, He2002

- 838-D: Five human MAbs against were derived from HIV-infected North American subjects after selection by the V3 RF peptide – 838-D was cross-reactive with V3 peptides from clade A and C, and could bind to 5/8 B clade V3 peptides – 50% neutralization of RF was obtained [Gorny1997]
- 838-D: Four primary isolates showed distinct patterns of sensitivity to neutralization by polyclonal sera or plasma and MAbs – BZ167 was the only isolate inhibited by all polyclonal sera and plasma tested, and was also neutralized by 8/17 MAbs, in particular anti-V3 loop (419-D, 447-52D, 782-D, and 838-D), anti-CD4bd (559/64-D, 654-D and 830-D and a cluster II of gp41 directed MAb (98-6) – isolates 92HT593 and 91US056 were neutralized by V3 loop (419-D, and 447-52D)and cluster II gp41 (98-6) MAbs at higher concentrations – US4 was neutralized by some of the polyclonal sera/plasma tested and not at all by MAbs individually or by a cocktail of ten MAbs consisting of 419-D, 447-52D, 782-D, 838-D, 559/64-D, 654-D, 450-D, 670-D, 1281-D and 98-6 [Hioe1997b]
- 838-D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – 838-D bound B clade virions but had limited cross-reactivity with other clades, with low levels of binding to A and D virions [Nyambi1998]
- 838-D: Review of clade specificity and anti-V3 HIV-1-Abs – this Ab showed strong binding to many A, B, C and F peptides, poor binding to D and E [Zolla-Pazner1999a]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 838-D: MAb peptide-reactivity pattern clustered with immunological related MAbs: 838, 782, 1027, 908, and 1006, all selected with RF V3 peptide – the core amino acids KSITK tended to be critical for reactivity in this group [Zolla-Pazner1999b]
- 838-D: Binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – V3 MAbs 447-52D, 838-D, and 1334 bound with a 7-10 fold preference for the oligomer [Gorny2000a]
- 838-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 838-D showed intermediate reactivity [Nyambi2000]
- 838-D: Called 838 – Transgenic mice carrying human genes allowing production of fully human MAbs were used to rapidly create a panel of anti-HIV gp120 MAb producing hybridomas by immunization with HIV SF162 gp120 – the previously described human MAbs 5145A(CD4BS) , 4117C (plus others, V3) and 697D (and SC258, V2) were used as controls [He2002]
- 838-D: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain [Zhang2002]

440	1006-15D (1006)	gp160 (307–312)	gp120 (RF)	KSITKG	no	HIV-1 infection	human (IgG1λ)

Ab type V3 **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny1997, Zolla-Pazner1999a, Zolla-Pazner1999b, Nyambi2000, He2002

- 1006-15D: Five human MAbs against were derived from HIV-infected North American subjects after selection by the V3 RF peptide – was somewhat cross-reactive with V3 peptides from clade A, C and other B clade V3 peptides, but not E clade [Gorny1997]
- 1006-15D: Review of clade specificity and anti-V3 HIV-1-Abs – this Ab showed strong binding to several B and F peptides, one C peptide, and some reactivity with A peptides – no binding was observed with D and E peptides [Zolla-Pazner1999a]
- 1006-15D: MAb peptide-reactivity pattern clustered with immunological related MAbs: 838, 782, 1027, 908, and 1006, all selected with RF V3 peptide – the core amino acids KSITK tended to be critical for reactivity in this group [Zolla-Pazner1999b]
- 1006-15D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 1006-15D showed strong cross-reactivity [Nyambi2000]
- 1006-15D: Called 1006 – Transgenic mice carrying human genes allowing production of fully human MAbs were used to rapidly create a panel of anti-HIV gp120 MAb producing hybridomas by immunization with HIV SF162 gp120 – the previously described human MAbs 5145A(CD4BS) , 4117C (plus others, V3) and 697D (and SC258, V2) were used as controls [He2002]

441	782-D (782)	gp160 (307–312)	Env (RF)	KSITKG	L	HIV-1 infection	human (IgG1λ)

Ab type V3 **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny1997, Hioe1997b, Zolla-Pazner1999a, Zolla-Pazner1999b, Nyambi2000

- 782-D: Five human MAbs against were derived from HIV-infected North American subjects after selection by the V3 RF peptide – 782-D was not cross-reactive with V3 peptides from clade A or E, but could bind to 3/8 B clade V3 peptides, and 1/2 C clade V3 peptides – 50% neutralization of RF was obtained [Gorny1997]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 782-D: Four primary isolates showed distinct patterns of sensitivity to neutralization by polyclonal sera or plasma and MAbs – BZ167 was the only isolate inhibited by all polyclonal sera and plasma tested, and was also neutralized by 8/17 MAbs, in particular anti-V3 loop (419-D, 447-52D, 782-D, and 838-D), anti-CD4bd (559/64-D, 654-D and 830-D and a cluster II of gp41 directed MAb (98-6) – isolates 92HT593 and 91US056 were neutralized by V3 loop (419-D, and 447-52D)and cluster II gp41 (98-6) MAbs at higher concentrations – US4 was neutralized by some of the polyclonal sera/plasma tested and not at all by MAbs individually or by a cocktail of ten MAbs consisting of 419-D, 447-52D, 782-D, 838-D, 559/64-D, 654-D, 450-D, 670-D, 1281-D and 98-6 [Hioe1997b]
- 782-D: Review of clade specificity and anti-V3 HIV-1-Abs – this Ab showed strong binding to several B and F peptides, one C peptide, and some reactivity with A and D peptides [Zolla-Pazner1999a]
- 782-D: MAb peptide-reactivity pattern clustered with immunological related MAbs: 838, 782, 1027, 908, and 1006, all selected with RF V3 peptide – the core amino acids KSITK tended to be critical for reactivity in this group [Zolla-Pazner1999b]
- 782-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 782-D showed intermediate reactivity [Nyambi2000]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
442	908-D (908, 908-12D)	gp160 (307–312)	gp120 (RF)	KSITKG	L	HIV-1 infection	human (IgG1λ)

Ab type V3 **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny1997, Zolla-Pazner1999a, Zolla-Pazner1999b, Nyambi2000

- 908-D: Five human MAbs against were derived from HIV-infected North American subjects after selection by the V3 RF peptide – 908-D was not cross-reactive with V3 peptides from clade E, but could bind to 6/8 B clade V3 peptides, 2/4 A clade, and 1/2 C clade – 50% neutralization of RF was obtained [Gorny1997]
- 908-D: Review of clade specificity and anti-V3 HIV-1-Abs – this Ab showed strong binding to several A, B, C and F peptides, and poor binding to E and D peptides [Zolla-Pazner1999a]
- 908-D: MAb peptide-reactivity pattern clustered with immunological related MAbs: 838, 782, 1027, 908, and 1006, all selected with RF V3 peptide – the core amino acids KSITK tended to be critical for reactivity in this group [Zolla-Pazner1999b]
- 908-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross -reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 908-D showed strong cross-reactivity, but achieved only 50% neutralization on 2/5 isolates tested [Nyambi2000]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
443	1027-15D (1027, 1027-D, 1027D)	gp160 (307–313)	Env (RF)	KSITKGP	no	HIV-1 infection	human (IgG1λ)

Ab type V3 **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny1997, Zolla-Pazner1999a, Zolla-Pazner1999b, Nyambi2000, Zhang2002

- 1027-15D: Five human MAbs against were derived from HIV-infected North American subjects after selection by the V3 RF peptide – 1027-15D was not cross-reactive with V3 peptides from clade A or E, but could bind to 3/8 B clade V3 peptides, and 1/2 C clade V3 peptides [Gorny1997]
- 1027-15D: Review of clade specificity and anti-V3 HIV-1-Abs – this Ab showed moderate binding to several B and F peptides, one C peptide, and was not reactivity with A, D and E peptides [Zolla-Pazner1999a]
- 1027-15D: MAb peptide-reactivity pattern clustered with immunological related MAbs: 838, 782, 1027, 908, and 1006, all selected with RF V3 peptide – the core amino acids KSITK tended to be critical for reactivity in this group [Zolla-Pazner1999b]
- 1027-15D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 1027-15D showed strong cross-reactivity [Nyambi2000]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 1027-15D: Called 1027-D – A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain [Zhang2002]					
444	F19.26-4	gp160 (307–319)	gp120 (312–324 LAI)	IRIQRGPGRAFVT	L	Vaccine	murine (IgG2aκ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* gp120 **Ab type** V3 **References** Boudet1994 • F19.26-4: Strain specific – used to raise anti-idiotype antibodies [Boudet1994]					
445	F19.48-3	gp160 (307–319)	gp120 (312–324 LAI)	IRIQRGPGRAFVT	L	Vaccine	murine (IgG2aκ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* gp120 **Ab type** V3 **References** Boudet1994 • F19.48-3: Strain specific – used to raise anti-idiotype antibodies [Boudet1994]					
446	F19.57-11	gp160 (307–319)	gp120 (312–324 LAI)	IRIQRGPGRAFVT	L (LAI)	Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* gp120 **Ab type** V3 **References** Boudet1991, Boudet1994, Boudet1995 • F19.57-11: MAb F19.57-11 is strain specific for LAI – used to raise anti-idiotype rabbit antibodies (called 57-B Ab2) [Boudet1994] • F19.57-11: Anti-anti-idiotypic antibodies (Ab3) were raised in BALBc mice that had greater breadth of reactivity than the original F19.57-11 (Ab3 could also recognize 1282 and SF2, with aa TRK(R or S)IYIGPGRA(WY or FH)T) [Boudet1995]					
447	M77	gp160 (307–320)	gp120 (IIIB)	IRIQRGPGRAFVTI	L	HIV-1 infection	human (IgG)
		Ab type V3 **Donor** Advanced BioScience Laboratories, Rockville, MD, commercial **References** Pal1992, diMarzo Veronese1992, diMarzo Veronese1993, Watkins1993, Cook1994, DeVico1995, Denisova1995, Watkins1996, Denisova2000 • M77: IIIB-specific MAb, immunoprecipitates deglycosylated form [diMarzo Veronese1992] • M77: Antibody binding to viral isolates from IIIB infected lab worker followed through time – A to T substitution resulted in the loss of neutralization and native gp120 binding, but not peptide binding [diMarzo Veronese1993] • M77: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – this MAb can inhibit gp120 binding to GalCer in vitro [Cook1994] • M77: Reacted with both reduced and non-reduced covalently cross-linked gp120-CD4 complex [DeVico1995] • M77: Conformational rearrangements upon binding of M77 to gp120 generates novel epitopes called metatopes [Denisova1995] • M77: Stated to be a murine MAb – a neutralization escape mutant (HXB2 A281V) was selected by growth of HXB2 in the presence of broadly neutralizing sera – M77 neutralization was only slightly reduced by this mutation [Watkins1993] • M77: Used M77 bound to gp120 as an immunogen – analysis of polyclonal and monoclonal (62 MAbs were generated) response suggests the M77-gp120 immunogen generated MAbs to more linear epitopes than gp120 alone or gp120 bound to CD4 [Denisova1996] • M77: Native M77 is highly strain specific, and V3 binding is primarily dependent on its heavy chain – a light chain switched Fab version of M77 could recognize HIV-1 strains that had substitutions on the left side of the V3 loop – R in GPGR is likely to be critical for binding [Watkins1996]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• M77: M77 is highly strain specific for IIIB, but anti-idiotypic Abs directed against M77 can in turn elicit an Ab response with expanded HIV cross-reactivity – this mechanism may serve to prolong the primary response and to counter-balance viral immune evasion by mutation [Denisova2000]					
448	SP.BAL114	gp160 (308–317)	gp120 (BAL)	SIHIGPGRAF	L		murine? (IgG2aκ)
		Ab type V3 **References** Arendrup1995 • Authors suggest that during in vivo immunoselection of escape virus, the V3 domain gains increasing resemblance to that of lab strains [Arendrup1995]					
449	SP.SF2:104	gp160 (308–317)	gp120 (SF2)	SIYIGPGRAF	L	HIV-1 infection	(IgG2aκ)
		Ab type V3 **References** Arendrup1993, Arendrup1995 • SP.SF2:104: Anti-V3 antibody that could neutralize primary virus isolated from a time point of neutralization resistance of autologous virus [Arendrup1993] • SP.SF2:104: Authors suggest that during in vivo immunoselection of escape virus, the V3 domain gains increasing resemblance to lab strains [Arendrup1995]					
450	polyclonal	gp160 (308–319)	gp120 (304–318 LAI)	RIHIGPGRAFYT		HIV-1 infection	human (IgG, IgM)
		Ab type V3 **References** Langedijk1995 • Polylconal sera from six individuals tested for reactivity against a panel of peptides based on autologous sequences provide evidence for immunological escape mutations in the tip of the V3 loop [Langedijk1995]					
451	19b	gp160 (308–320)	gp120	-I----G--FY-T	L	HIV-1 infection	human (IgG1)
		Ab type V3 **Donor** James Robinson, University of Connecticut, Storrs **References** Scott1990, Moore1994b, Moore1994a, Sattentau1995a, Moore1995c, Moore1995a, Moore1995b, Gauduin1996, Wu1996, Trkola1996a, D'Souza1997, Binley1997a, Fouts1997, Ugolini1997, Boots1997, Parren1997c, Mondor1998, Parren1998a, Trkola1998, Binley1999, Park2000, Kolchinsky2001, Schulke2002, Zhang2002, Poignard2003 • 19b: V3 loop binding MAb that is more broadly clade cross-reactive than most (binds to 19/29 clade B and 10/12 clade E gp120s) [Moore1994b] • 19b: Competition studies with human sera from seroconverting individuals showed that anti-CD4 BS antibodies can arise very early in infection, comparable or prior to anti-V3 antibodies [Moore1994a] • 19b: Formalin inactivation of virus at 0.1% formalin for 10 hours at 4 degrees was optimal for inactivation of virus while maintaining epitope integrity [Sattentau1995c] • 19b: Binds to some gp120s from clades A,B,C,E, and F – weakly neutralized some B and one C clade virus [Moore1995c] • 19b: Despite broad gp120 binding reactivity, not broadly neutralizing [Moore1995a] • 19b: Review: more broadly cross-reactive than anti-V3 tip MAb 447-D [Moore1995b] • 19b: Not as effective as IgG1b12 at neutralization ex vivo of virus direct from plasma of HIV-1 infected individuals [Gauduin1996] • 19b: MIP-1alpha binding to CCR-5 expressing cells can be inhibited by gp120-sCD4 – binding of 19b blocks this inhibition [Wu1996] • 19b: Inhibits gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study [Trkola1996a] • 19b: In a multilaboratory blinded study, failed to consistently neutralize any of nine B clade primary isolates – there were four sequences with variations in the defined epitope among the 9 isolates tested [D'Souza1997] • 19b: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric Env binding – 19b bound monomer, did not bind oligomer or neutralize JRFL [Fouts1997] • 19b: Viral binding inhibition by 19b was weakly correlated with neutralization (all other neutralizing MAbs tested showed some correlation except 2F5) [Ugolini1997]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 19b: Abs that recognize discontinuous epitopes can identify mimotopes from a phage peptide display library – 19b has an epitope involving the tip of the V3 loop, with 5 or 6 essential amino acids distributed within a 12 amino acid stretch – the previously determined binding site was confirmed -I—-G–FY-T and some tolerated variants described, the I can be I, V, or L, the Y can be Y, F, or W – probably a beta-turn is required for FY or FF binding, but WY in can bind with out the context of the turn [Boots1997]
- 19b: Neutralizes TCLA strains but not primary isolates [Parren1997c]
- 19b: Used as a control in this Hx10 binding and neutralizing MAb study because 19b does not bind to Hx10 [Mondor1998]
- 19b: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren1998a]
- 19b: No detectable neutralizing activity among primary isolates with different co-receptor usage – some neutralization of TCLA strains [Trkola1998]
- 19b: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes [Binley1999]
- 19b: Six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20-100 fold more efficient at neutralizing the sensitive form but 19b was an exception and required around 950 ng/ml to neutralize either form [Park2000]
- 19b: Mutations in two glycosylation sites in the V2 region of HIV-1 ADA at positions 190 and 197 (187 DNTSYRLINCNTS 199) cause the virus to become CD4-independent and able to enter cells through CCR5 alone – these same mutations tended to increase the neutralization sensitivity of the virus, including to 19b [Kolchinsky2001].
- 19b: Ab binding characteristics of SOS gp140 were tested using SPR and RIPA – SOS gp140 is gp120-gp41 bound by a disulfide bond – NAbs 2G12, 2F5, IgG1b12, CD4 inducible 17b, and 19b bound to SOS gp140 better than uncleaved gp140 (gp140unc) and gp120 – non-neutralizing MAbs 2.2B (binds to gp41 in gp140unc) and 23A (binds gp120) did not bind SOS gp140 [Schulke2002]
- 19b: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain [Zhang2002]
- 19b: Virion capture assays are not a good preditor of neutralization, and the presentation of epitopes using this assay seems to be different from that of functional Envelope spikes on primary isolates – F105 and b6 could efficiently block the b12-mediated capture of infectious virions in a virus capture, but did not inhibit b12 neutralization – while b12 was potent at neutralizing the three primary virions JR-CSF, A DA, and 89.6, the Abs F105, 19b, and Fab b6 were overall very poor neutralizers [Poignard2003]

452	4G10	gp160 (308–322)	gp120 (308–322 LAI)	RIQRGPGRAFVTGK		Vaccine	murine

Vaccine *Vector/Type:* HBcAg fusion *HIV component:* V3
Ab type V3 **Donor** Dr. Albrecht von Brunn, Max-von-Pettenkofer-Institut, Ludwig-Maximilians-Universitat Munchen, Germany
References vonBrunn1993

- 4G10: A 25 amino acid V3-loop sequence fused to HBcAg enhanced V3 immunogenicity [vonBrunn1993]
- 4G10: NIH AIDS Research and Reference Reagent Program: 2534

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
453	5F7	gp160 (308–322)	gp120 (308–322 LAI)	RIQRGPGRAFVTGK		Vaccine	murine
		Vaccine *Vector/Type:* HBcAg fusion *HIV component:* V3 **Ab type** V3 **Donor** Dr. Albrecht von Brunn, Max-von-Pettenkofer-Institut, Ludwig-Maximilians-Universitat Munchen, Germany **References** vonBrunn1993 • 5F7: A 25 amino acid V3-loop sequence fused to HBcAg enhanced V3 immunogenicity [vonBrunn1993] • 5F7: NIH AIDS Research and Reference Reagent Program: 2533						
454	G3-523	gp160 (308–322)	gp120 (308–322)	RIQRGPGRAFVTIGK			murine
		Ab type V3 **References** Matsushita1988, Jagodzinski1996 • G3-523: The sulfated polysaccharide curdlan sulfate (CRDS) binds to the Envelope of T-tropic viruses and neutralizes virus – CRDS inhibits G3-523 binding [Jagodzinski1996]					
455	MN215	gp160 (308–322)	gp120 (MN)	RIHIGPGRAFYTTKN	L	HIV-1 infection	human (IgG1)
		Ab type V3 **References** Schutten1995b • MN215: Minimum epitope for MAB using the Dutch consensus is AFYTTGE, different than defined for MN – generated by EBV transformation of PBMC – displayed higher affinity for NSI than for SI glycoproteins – amino acids HIGP were essential for binding [Schutten1995b]					
456	Nea 9301	gp160 (308–323)	gp120 (IIIB)	RIQRGPGRAFVTIGKI			murine
		Ab type V3 **Donor** Dupont, commercial **References** Wagner1996					
457	4117C	gp160 (309–315)	gp120	IXIGPGR	L	HIV-1 infection	human (IgG1λ)
		Ab type V3 **References** Tilley1991b, Tilley1992, diMarzo Veronese1993, Pinter1993a, Pinter1993b, Alsmadi1998, He2002 • 4117C: Potent neutralizing activity against MN, SF-2, and NY-5 – synergy with CD4BS MAb 1125H [Tilley1991b] • 4117C: Neutralizes SF2 and MN synergistically combined with anti-CD4 binding site discontinuous MAb [Pinter1993a, Tilley1992] • 4117C: Binds V3 loop – does not immunoprecipitate soluble gp120, does react with gp120 on intact virions [Pinter1993b] • 4117C: A study of 6 anti-Env MAbs and their ability to bind or direct ADCC against target cells infected with IIIB, MN, SF-2, and RF – bound and directed lysis against MN and SF2, but not IIIB and RF [Alsmadi1998] • 4117C: Transgenic mice carrying human genes allowing production of fully human MAbs were used to rapidly create a panel of anti-HIV gp120 MAb producing hybridomas by immunization with HIV SF162 gp120 – the previously described human MAbs 5145A(CD4BS) , 4117C (plus others, V3) and 697D (and SC258, V2) were used as controls [He2002]					
458	419-D (419, 419D)	gp160 (309–315)	gp120 (MN)	IHIGPGR	L	HIV-1 infection	human (IgG1λ)
		Ab type V3 **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center) **References** Karwowska1992b, Gorny1993, Spear1993, Fontenot1995, Hioe1997b, Nyambi1998, Zolla-Pazner1999a, Zolla-Pazner1999b, Nyambi2000, He2002 • 419-D: MN, NY5 and SF2 strain specific, does not cross-react with RF, CDC4, WM52 or HXB2 [Karwowska1992b] • 419-D: Neutralizes MN – binds SF2: IYIGPGR [Gorny1993] • 419-D: Mediated deposition of complement component C3 on HIV infected cells, enhanced by second Ab binding, rabbit anti-human IgG [Spear1993]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 419-D: Four primary isolates showed distinct patterns of sensitivity to neutralization by polyclonal sera or plasma and MAbs – BZ167 was the only isolate inhibited by all polyclonal sera and plasma tested, and was also neutralized by 8/17 MAbs, in particular anti-V3 loop (419-D, 447-52D, 782-D, and 838-D), anti-CD4bd (559/64-D, 654-D and 830-D and a cluster II of gp41 directed MAb (98-6) – isolates 92HT593 and 91US056 were neutralized by V3 loop (419-D, and 447-52D)and cluster II gp41 (98-6) MAbs at higher concentrations – US4 was neutralized by some of the polyclonal sera/plasma tested and not at all by MAbs individually or by a cocktail of ten MAbs consisting of 419-D, 447-52D, 782-D, 838-D, 559/64-D, 654-D, 450-D, 670-D, 1281-D and 98-6 [Hioe1997b]
- 419-D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – 419-D bound to 3/4 B clade virions, and to D clade MAL [Nyambi1998]
- 419-D: Review of clade specificity and anti-V3 HIV-1-Abs – epitope is described as KRIHIGP [Zolla-Pazner1999a]
- 419-D: MAb peptide-reactivity pattern clustered with immunological related MAbs: 1334, 419, 504, 447, 453 and 537 – the core amino acids GP tended to be critical for reactivity in this group [Zolla-Pazner1999b]
- 419-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 419-D showed intermediate reactivity, and no neutralization when tested against five strains – discrepancy between the epitope as described in earlier papers and as described here, KRIHIGP [Nyambi2000]
- 419-D: Called 419 – Transgenic mice carrying human genes allowing production of fully human MAbs were used to rapidly create a panel of anti-HIV gp120 MAb producing hybridomas by immunization with HIV SF162 gp120 – the previously described human MAbs 5145A(CD4BS) , 4117C (plus others, V3) and 697D (and SC258, V2) were used as controls [He2002]

459	453-D (453)	gp160 (309–315)	gp120 (MN)	IHIGPGR	L	HIV-1 infection	human (IgG1λ)

Ab type V3 **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny1991, Gorny1993, VanCott1994, Fontenot1995, Zolla-Pazner1999a, Zolla-Pazner1999b, Nyambi2000

- 453-D: Neutralizes MN – binds SF2: IYIGPGR – specificity: MN, SF2, NY5, RF [Gorny1993]
- 453-D: Moderate homologous neutralization, moderately slow dissociation rate [VanCott1994]
- 453-D : Called 453, epitope described as KRIHIGPGR – the tip of the V3 loop was presented in a mucin backbone – higher valency correlates with stronger affinity constant [Fontenot1995]
- 453-D: Review of clade specificity and anti-V3 HIV-1-Abs [Zolla-Pazner1999a]
- 453-D : MAb peptide-reactivity pattern clustered with immunological related MAbs: 1334, 419, 504, 447, 453 and 537 – the core amino acids GP tended to be critical for reactivity in this group – MAb 268, with a previously defined core epitope identical to 453 (HIGPGR), was not part of this reactivity group, illustrating that context can be critical [Zolla-Pazner1999b]
- 453-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 453-D showed intermediate reactivity [Nyambi2000]

460	504-D (504, 504-10D)	gp160 (309–315)	gp120 (MN)	IHIGPGR	L	HIV-1 infection	human (IgG1κ)

Ab type V3 **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny1993, Zolla-Pazner1999a, Zolla-Pazner1999b, Nyambi2000

- 504-D – Neutralizes MN – binds SF2: IYIGPGR [Gorny1993]
- 504-D: Review of clade specificity and anti-V3 HIV-1-Abs [Zolla-Pazner1999a]
- 504-D: MAb peptide-reactivity pattern clustered with immunological related MAbs: 1334, 419, 504, 447, 453 and 537 – the core amino acids GP tended to be critical for reactivity in this group [Zolla-Pazner1999b]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 504-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 504-D showed weak reactivity [Nyambi2000]					
461	83.1 (MAb 83.1)	gp160 (309–315)	gp120 (SF2)	IYIGPGR	L	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* peptide *Strain:* MN *HIV component:* V3 **Ab type** V3 **Donor** Mary White-Scharf, Repligen Corporation, Cambridge, MA **References** White-Scharf1993, Potts1993, Jelonek1999, Keller1999, Binley1999 • 83.1: Neutralizes SF2 [White-Scharf1993] • 83.1: Study of synergism of neutralization and binding comparing F105 and sCD4 with the V3 MAbs: 50.1, 59.1, 83.1, and 58.2 – synergy was observed, and the data suggest that binding of one ligand (F105) can increase the binding of the second (e. g. V3 loop MAbs) due to conformational changes [Potts1993] • 83.1: Maternally transferred anti-V3 loop MAb selectively inhibits the anti-V3 loop Ab component of the IgG response to rgp120 SF2 in 21 day old BALBc mice [Jelonek1999] • 83.1: 19 day old mice injected with 83.1 have a shift in IgG1 response away from the V3 loop upon vaccination, without decreasing the total IgG anti-gp120 response, suggesting that prior treatment with a MAb can mask immunogenic sites and shift the immune response to vaccination [Keller1999] • 83.1: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes [Binley1999]			
462	5023B	gp160 (309–316)	gp120 (309–316 BH10)	IQRGPGra	no	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* peptide *Strain:* BH10 *HIV component:* V3 **Ab type** V3 **References** Langedijk1991 • 5023B: Generation and fine mapping of murine MAbs [Langedijk1991]					
463	F58/D1 (F58)	gp160 (309–316)	gp120 (IIIB)	IxxGPGRA	L	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* virus derived protein *HIV component:* gp120 **Ab type** V3 **References** Akerblom1990, Broliden1991, Moore1993c, Millar1998, Jackson1999 • F58/D1: Binding to native gp120 1-3 fold greater than to denatured – 314G/W substitution abolishes binding, changes outside the loop have little effect [Moore1993c] • F58/D1: The interaction of a 17-amino-acid neutralizing microantibody (MicroAB) based on F58 and HIV-1 env was studied by electrospray ionization mass spectrometry [Millar1998] • F58/D1: A 17 amino acid MicroAB was made from the third complementarity-determining region of the heavy chain of MAb – F58 neutralized 5x's more efficiently in terms of mass than the original MAb, 32-fold less on a molar basis – neutralization does not involve initial attachment, but fusion and events in early infection [Jackson1999]					
464	P1/D12	gp160 (309–316)	gp120	IxxGPGRA	L	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* virus derived protein *Strain:* IIIB *HIV component:* gp120					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		Ab type V3 **References** Akerblom1990, Moore1993c • P1/D12: Binding to native gp120 1-3 fold greater than to denatured – 314G/W substitution abolishes binding, changes outside the loop have little effect [Moore1993c]					
465	P4/D10 (P4D10)	gp160 (309–316)	gp120	IxxGPGRA	L	Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* virus derived protein *Strain:* IIIB *HIV component:* gp120 **Ab type** V3 **References** Akerblom1990, Broliden1990, Broliden1991, Marks1992, Moore1993c, Arendrup1993, Hinkula1994, Jacobson1998, Schonning1998, Schonning1999 • P4/D10: Neutralizing and ADCC activity [Broliden1990] • P4/D10: Variable domain sequenced and is identical to F58/H3 [Marks1992] • P4/D10: Binding to native gp120 3 fold greater than to denatured – 314G/W substitution abolishes binding, changes outside the loop have little effect [Moore1993c] • P4/D10: Primary isolates from different time points from one individual were not susceptible to neutralization by P4/D10 [Arendrup1993] • P4/D10: Used for passive immunotherapy in four late-stage HIV-infected patients – the serum level of p24 did not decrease in any of these four – see also MAb F58/H3 [Hinkula1994] • P4/D10: Review of passive immunotherapy, summarizing [Hinkula1994] in relation to other studies [Jacobson1998] • P4/D10: Called P4D10 – In a study of the influence of the glycan at position 306 of the V3 loop on MAb recognition, anti-V3 MAbs were found to neutralize an HIV-BRU mutant virus that lacks the V3 loop glycan more efficiently than HIV-BRU – Ab binding site was suggested to be 314-323 of BRU [Schonning1998] • P4/D10: Called P4D10 – the stoichiometry of MAb neutralization was tested and the data indicated that binding for neutralization was was incremental not all or none, i.e., each envelope oligomer binds a single MAb and each Env oligomer bound reduces the chances of infection – MAb BC1071 was used for virion quantification – P4D10 binds only to Env with a glycosylation site mutation at the base of the V3 loop A308T [Schonning1999]			
466	IIIB-13 V3 (1044-13 IIIB-V3-13 1727)	gp160 (309–317)	gp120 (308–316 IIIB)	IQRGPGRAF	L	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* peptide *Strain:* IIIB **Ab type** V3 **References** Laman1992, Laman1993, D'Souza1994, Watkins1993, Chakrabarti2002, Zhang2002 • IIIB-13 V3: Also known as 1044-13 and as IIIB-V3-13 (J. P. Moore, per. comm.) • IIIB-13 V3: Neutralizes IIIB but not MN [Laman1992] • IIIB-13 V3: Included in a panel of antibodies used in a multi-lab study for antibody characterization and assay comparison, some neutralization of strains other than IIIB [D'Souza1994] • IIIB-13 V3: Called IIIB-V3-13 – a neutralization escape mutant (HXB2 A281V) was selected by growth of HXB2 in the presence of broadly neutralizing sera – IIIB-V3-13 neutralization was only slightly reduced by this mutation [Watkins1993] • IIIB-13 V3: Called 1727: Used as a standard for comparing immune responses to modified gp140 (gp140deltaCFI), with C-term mutations intended to mimic a fusion intermediate and stabilize trimer formation – experiment showed enhanced humoral immunity without diminishing the CTL response in mice injected with a DNA vaccine [Chakrabarti2002] • IIIB-13 V3: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain [Zhang2002]			

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• IIIB-13 V3: UK Medical Research Council AIDS reagent: ARP3046 • IIIB-13 V3: NIH AIDS Research and Reference Reagent Program: 1727					
467	IIIB-34 V3 (IIIB-V3-34)	gp160 (309–317)	gp120 (308–316 IIIB)	IQRGPGRAF	L	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* peptide *Strain:* IIIB **Ab type** V3 **References** Laman1992, Laman1993 • IIIB-34 V3: Neutralizes IIIB but not MN – QXGPG are critical amino acids for binding by Pepscan analysis [Laman1992] • IIIB-34 V3: Called IIIB-V3-34 – IIIB strain specific neutralization – binding is reduced somewhat by DTT or SDS-DTT, enhanced by NP40, but binds to native and denatured gp120 [Laman1993] • IIIB-34 V3: UK Medical Research Council AIDS reagent: ARP3047					
468	A47/B1	gp160 (309–318)	gp120 (307–316 IIIB)	IQRGPGRAFV	L	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* protein *Strain:* IIIB *HIV component:* gp120 **Ab type** V3 **References** Akerblom1990					
469	D59/A2	gp160 (309–318)	gp120 (307–316 IIIB)	IQRGPGRAFV	L	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* protein *Strain:* IIIB *HIV component:* gp120 **Ab type** V3 **References** Akerblom1990					
470	G44/H7	gp160 (309–318)	gp120 (307–316 IIIB)	IQRGPGRAFV	L	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* protein *Strain:* IIIB *HIV component:* gp120 **Ab type** V3 **References** Akerblom1990					
471	M096/V3	gp160 (309–318 + 329–338)	gp120 (dis 309–318)	IQRGPGRAFV+AHCNISRAKW		in vitro stimulation	human (IgM)
		Ab type V3 **References** Ohlin1992 • M096: Generated in response to IIIB Env 286-467 upon in vitro stimulation of uninfected-donor lymphocytes, and binds to two peptides: 309-318 + 329-338 [Ohlin1992]					
472	μ5.5 (5.5, mu5.5, Rmu5.5)	gp160 (309–319)	gp120 (MN)	IHIGPGRAFYT	L P		murine (IgG1κ)
		Ab type V3 **References** Maeda1992, Okamoto1998 • mu5.5: sCD4 causes loss of IIIB type-specificity for MAb 0.5beta, allowing binding and neutralization of MN, in contrast to MAb mu5.5 [Maeda1992] • mu5.5: Rmu5.5 is a humanized antibody of mouse MAb m5.5 – neutralized primary isolates with similar V3 loops – passive transfer of MAb to SCID-hu or hu-PBL-SCID mice conferred protection [Okamoto1998]					
473	loop 2 (Loop 2, IgG1 Loop 2)	gp160 (309–320)	gp120	SISGPGRAFYTG	L	HIV-1 infection	human Fab
		Ab type V3 **Donor** D. Burton, Scripps Research Institute, La Jolla, CA **References** Barbas III1993, Moore1994b, Wu1996, Ditzel1997, Ugolini1997, Parren1997c, Parren1997a, Mondor1998, Parren1998a, Sullivan1998a • loop2: Also known as Loop 2, IgG1 Loop 2 was a obtained by engineering Fab loop2 into an IgG1 molecule					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- loop 2: Sequences of the heavy and light chain Fab variable regions were generated [Barbas III1993]
- loop 2: Called Loop 2 – shows modest cross-reactivity among B clade gp120s, little outside B clade [Moore1994b]
- loop 2: MIP-1alpha binding to CCR-5 expressing cells can be inhibited by gp120-sCD4 – binding of loop 2 blocks this inhibition [Wu1996]
- loop 2: Binds to gp120 from MN and SF2 but not LAI [Ditzel1997]
- loop 2: Viral binding inhibition by loop 2 MAb or Fab was correlated with neutralization (all other neutralizing MAbs tested showed some correlation except 2F5) [Ugolini1997]
- loop 2: Epitope is suggested to be GPGRAF – binds to 10/17 US clade B monomeric gp120s – IgG1 form can neutralize MN and 2 primary isolates tested [Parren1997a]
- loop 2: Neutralizes TCLA strains but not primary isolates [Parren1997c]
- loop 2: The rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142-10 > DA48 > L17) was markedly different than Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142-10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope – binding affinity of divalent IgG1 loop 2 is only 2-fold greater than monovalent Fab loop 2, suggesting the IgG1 form may bind with only one arm [Parren1998a]
- loop 2: The HIV-1 virus YU2 entry can be enhanced by MAbs binding to the CD4BS, V3 loop, and CD4i epitopes – the activation for this enhanced entry state could be conferred on HxB2 by introducing the YU2 V3 loop, or the YU2 V3 and V1/V2 loops – a similar effect is observed by sub-neutralizing concentrations of sCD4 and the effect is dependent of CCR5 – loop 2 enhances YU2 at concentrations up to 20 ug/ml [Sullivan1998a]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
474	268-D (268-11-D-IV, 268D, 268, 268-11D, 268-10D, MAb 268, 268-10-D, ARP3024)	gp160 (310–315)	gp120 (MN)	HIGPGR	L	HIV-1 infection	human (IgG1λ)

Ab type V3 **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny1991, D'Souza1991, Karwowska1992b, Gorny1993, Spear1993, VanCott1994, Stamatatos1995, Zolla-Pazner1995a, Fontenot1995, McKeating1996b, Wisnewski1996, Hioe1997b, Stamatatos1997, LaCasse1998, Zolla-Pazner1999a, Zolla-Pazner1999b, Beddows1999, Oggioni1999, Laisney1999, Hioe2000, Nyambi2000, Park2000, York2001, Vella2002, Zhang2002

- 268-D: Called 268-11-D-IV – strain specific weakly neutralizing [D'Souza1991]
- 268-D: Reacts with MN, NY5, CDC4, RF and SF2, does not cross-react with WM52 or HXB2 [Karwowska1992b]
- 268-D: Neutralizes MN – binds SF2: YIGPGR – specificity: MN, SF2, NY5, RF, CDC4 [Gorny1993]
- 268-D: Mediated deposition of complement component C3 on HIV infected cells, but not in the presence of sCD4 [Spear1993]
- 268-D: Moderate dissociation rate and homologous neutralization titer [VanCott1994]
- 268-D: Serotyping study using flow-cytometry, if H of HIGPGR was substituted in virus, 268-D did not bind [Zolla-Pazner1995a]
- 268-D: The binding of conformation-dependent anti-V2, anti-V3, and anti-CD4BS MAbs to monomeric and virion-associated gp120 from HIV-1 isolates with differences in cell tropism was studied – V3 loop epitopes were less accessible to Ab binding on the virion surface than in the gp120 monomer, particularly for macrophage-tropic isolates SF162 and SF128a, relative to T-cell tropic SF2 – sCD4 association with gp120 did not influence the binding of 268-D to virion-associated gp120, although sCD4 binding did alter epitope exposure for other anti-V3 MAbs [Stamatatos1995]
- 268-D: Failed to neutralize HXB2 and chimeric virus with gp120 from primary isolates in an HXB2 background [McKeating1996b]
- 268-D: 268-D is V H4 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals [Wisnewski1996]
- 268-D: Poor reactivity against HIV-1 isolates SF162 and SF128A and no neutralization, in contrast to MAbs 391/95-D and 257-D [Stamatatos1997]
- 268-D: A T-cell line-adapted (TCLA) derivative of SI primary isolate 168P acquired the ability to be neutralized by anti-V3 MAbs – the primary isolate could use either CCR5 or CXCR4, and was not neutralized when infection was directed via either pathway, however the TCLA derivative uses CXCR4 only and is neutralized [LaCasse1998]
- 268-D: Review of clade specificity and anti-V3 HIV-1-Abs [Zolla-Pazner1999a]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 268-D: Peptide reactivity pattern clustered with immunological related MAbs: 1108, 386, 268, 311, 257, 694.8 – the amino acids HI tended to be critical for reactivity in this group – MAb 453, with an identical core epitope to 268 based on prior experiments (HIGPGR), was not part of this reactivity group, illustrating that context can be critical [Zolla-Pazner1999b]
- 268-D: rgp120 derived from a R5X4 subtype B virus, HIV-1 W61D, was used to vaccinate healthy volunteers and the resulting sera were compared with sera from HIV-1 positive subjects and neutralizing MAbs – 268-D bound rgp120 W61D but could only neutralize the W61D isolate following T-cell line adaptation [Beddows1999]
- 268-D: Called 268-11D – Study of a live-vector mucosal vaccine that expresses HIV-1 V3 domains using the bacterium Streptococcus gordonii which can express heterologous Ag and can colonize the oral cavity and vagina of mice – 268-D and 257-D recognized S. gordonii expressing the V3 domain of MN – the vaccine stimulated V3-specific IgG2a in mice [Oggioni1999]
- 268-D: Called MAb 268 – To identify potential mimotopes of V3, a hexapeptide phage library was screened with MAb 268 – two hexamers were identified, HLGPGR or KAIHRI that bind to 268 with the same binding site as the V3 loop and inhibit 268 MN gp120 – KLH conjugated hexamer KAIHRI stimulates Abs in rabbits that cross-react with ML gp120 [Laisney1999]
- 268-D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – CD4BS MAbs or serum Ig from HIV+ individuals inhibited proliferative responses of gp120 specific T cells – V3 MAbs 447-52-D and 268-10-D did not effect proliferation [Hioe2000]
- 268-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 268-D showed weak reactivity [Nyambi2000]
- 268-D: Called 268D – six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20-100 fold more efficient at neutralizing the sensitive form – the mutation L544P reduced binding of all MAbs against gp120 by causing conformational changes [Park2000]
- 268-D: Abs against the V3 loop (50.1, 58.2, 59.1, 257-D, 268-D, 447-52D), CD4BS (IgG1b12, 559-64D, F105), CD4i (17b), and to gp41 (2F5, F240) each showed similar binding efficiency to Env derived from related pairs of primary and TCLA lines (primary: 168P and 320SI, and TCLA: 168C and 320SI-C3.3), but the TCLA lines were much more susceptible to neutralization suggesting that the change in TCLA lines that make them more susceptible to NAbs alters some step after binding – one of the TCLA V3 viruses 320SI-C3.3 shows reduced binding with this MAb, the sequence of the epitope in 320SI is HIGPGR and in 320SI-C3.3 is RIGPGR [York2001]
- 268-D: Called ARP3024: Herpesvirus saimiri-immortalized CD4+ T lymphocytes (HVS T cells) were used to isolate virus and perform HIV-1 neutralization assays, and compared with a standard PBMC protocol – neutralization sensitivities to a panel of MAbs and to homologous or heterologous plasma/sera were similar for HVS T cells (CN-2 cells) and PBMCs [Vella2002].
- 268-D: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera—2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5—thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain [Zhang2002].
- 268-D: UK Medical Research Council AIDS reagent: ARP3024
- 268-D: NIH AIDS Research and Reference Reagent Program: 1511

475	386-D (386, 386-10D, 386D)	gp160 (310–315)	gp120 (MN)	HIGPGR	L	HIV-1 infection	human (IgG1λ)

Ab type V3 **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Karwowska1992b, Gorny1993, VanCott1994, Fontenot1995, Zolla-Pazner1999a, Zolla-Pazner1999b, Nyambi2000

- 386-D: Neutralizes MN – binds SF2: YIGPGR – specificity: MN, SF2, NY5, RF, CDC4 [Gorny1993]
- 386-D: Slow dissociation rate, potent homologous neutralization [VanCott1994]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 386-D: Review of clade specificity and anti-V3 HIV-1-Abs [Zolla-Pazner1999a] • 386-D: Peptide reactivity pattern clustered with immunological related MAbs: 1108, 386, 268, 311, 257, 694.8 – the amino acids HI tended to be critical for reactivity in this group [Zolla-Pazner1999b] • 386-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 386-D showed intermediate reactivity [Nyambi2000]					
476	5042A	gp160 (310–315)	gp120 (310–315 BH10)	QrGPGR	L	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* peptide *Strain:* BH10 *HIV component:* V3 **Ab type** V3 **References** Langedijk1991, Gorny1991 • 5042A: Generation and fine mapping of murine MAbs [Langedijk1991]					
477	5042B	gp160 (310–315)	gp120 (310–315 BH10)	QRGPGr	no	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* peptide *Strain:* BH10 *HIV component:* V3 **Ab type** V3 **References** Langedijk1991 • 5042B: Generation and fine mapping of murine MAbs [Langedijk1991]					
478	418-D (418, 418D)	gp160 (310–316)	gp120 (MN)	HIGPGRA	L	HIV-1 infection	human (IgG1κ)
		Ab type V3 **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center) **References** Karwowska1992b, Gorny1993, Zolla-Pazner1999a, Zolla-Pazner1999b, Nyambi2000, Zhang2002 • 418-D: MN strain specific, does not cross-react with SF2, NY5, RF, CDC4 WM52 or HXB2 [Karwowska1992b] • 418-D: Neutralizes MN, does not bind to SF2 or HXB2 [Gorny1993] • 418-D: Review of clade specificity and anti-V3 HIV-1-Abs [Zolla-Pazner1999a] • 418-D: Called 418 – MAb peptide-reactivity pattern clustered with immunological related MAbs: 391.5, 412 and 418, all selected with MN V3 peptide – the core amino acids HIGPGR tended to be critical for reactivity in this group [Zolla-Pazner1999b] • 418-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 418-D showed intermediate reactivity [Nyambi2000] • 418-D: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain [Zhang2002]					
479	5021	gp160 (310–316)	gp120	QrGPGRa	L	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* peptide *Strain:* BH10 *HIV component:* V3 **Ab type** V3 **References** Durda1988, Durda1990, Langedijk1991, Moore1993c • 5021: Generation and fine mapping of murine MAbs [Langedijk1991] • 5021: Binding to native gp120 100-300 fold greater than to denatured – 314G/W substitution abolishes binding, changes outside the loop have little effect [Moore1993c]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
480	5025B	gp160 (310–316)	gp120 (310–316 BH10)	QRGPGra	no	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* peptide *Strain:* BH10 *HIV component:* V3 **Ab type** V3 **References** Langedijk1991 • 5025B: Generation and fine mapping of murine MAbs [Langedijk1991]					
481	5042	gp160 (310–316)	gp120	QRGPGRA	L	Vaccine	murine
		Vaccine *Vector/Type:* peptide **Ab type** V3 **References** Durda1988, Durda1990, Moore1993c • 5042: Binding to native gp120 100-300 fold greater than to denatured – 314G/W substitution abolishes binding, changes outside the loop have little effect [Moore1993c]					
482	110.3	gp160 (310–317)	gp120 (308–328 BRU)	QRGPGRAF	L	Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* infected-cell lysate *Strain:* BRU *HIV component:* virus **Ab type** V3 **References** Thomas1988, Evans1989, Langedijk1992, Pirofski1993, Connelly1994 • 110.3: Included as a control [Evans1989] • 110.3: MAb variable region sequenced – heavy chain: V 7138(40), D deletion, J H4 – light chain: V kappa21(47), J kappa2 [Pirofski1993] • 110.3: An anti-idiotypic MAb generated against 110.3 both mimics and binds to V3, suggesting that the V3 loop may associated with itself [Connelly1994]					
483	110.4	gp160 (310–317)	gp120 (308–328 BRU)	QRGPGRAF	L	Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* infected-cell lysate *Strain:* BRU *HIV component:* virus **Ab type** V3 **Donor** Genetic Systems Corp, Seattle WA, E. Kinney-Thomas **References** Thomas1988, Thali1992b, Langedijk1992, Thali1993, Pirofski1993, Arendrup1993, Thali1994, Boudet1994, Connelly1994, McDougal1996, Valenzuela1998, Cao1997b, Guillerm1998 • 110.4: 313 P/S substitution in the V3 region disrupts binding [Thali1992b] • 110.4: MAb variable region sequenced – heavy chain: V 3660-SB32, D closest to DSP2.3, 2.4 and .6, J H2 – light chain: V kappa21, J kappa2 [Pirofski1993] • 110.4: Primary isolates from different time points from one individual were not susceptible to neutralization by 110.4 [Arendrup1993] • 110.4: gp41 mutation that confers resistance to neutralization by anti-CD4 binding site antibodies does not reduce neutralizing efficiency of this V3 region MAb [Thali1994] • 110.4: An anti-idiotypic MAb generated against 110.3 also blocks binding of 110.4 [Connelly1994] • 110.4: Neutralizes HIV-1 LAI [McDougal1996] • 110.4: Neutralization of LAI in CEM cells by anti-V3 MAbs 110.4 and N11-20 is through inhibition of viral binding to the cell [Valenzuela1998] • 110.4: Virus with the V1-V2 loop deleted was viable and more susceptible to neutralization by CD4i MAb 17b, and anti-V3 MAbs 1121, 9284, and 110.4, but not to and CD4BS MAb F105 or sCD4 [Cao1997b] • 110.4: Used for flow cytometry in a study of the anti-CD4, CDR3 loop MAb called 13B8.2, in a study of HIV-1 induced programmed cell death [Guillerm1998]					
484	110.5	gp160 (310–317)	gp120 (308–328 BRU)	QRGPGRAF	L	Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* infected-cell lysate *Strain:* BRU *HIV component:* virus **Ab type** V3 **Donor** E. Kinney-Thomas or Genetic Systems, Seattle WA					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

References Thomas1988, Moore1990b, Cordell1991, Sattentau1991, Langedijk1992, McKeating1992a, Pirofski1993, Moore1993c, Thali1993, Klasse1993a, Sattentau1995c, Sattentau1995b, Moore1996, Poignard1996a, McDougal1996, Jeffs1996, Binley1997a, Ugolini1997, Parren1998a

- 110.5: Did not induce dissociation of gp120, as sCD4 did – discrepancy with [Poignard1996a], that was suggested to be due to MAb interference with detection, as the gp120-MAb complex was denatured in the Poignard study [Moore1990b]
- 110.5: Binding insensitive to gp120 reduction [Cordell1991]
- 110.5: Two fold increase in binding to gp120 in the presence of bound sCD4 [Sattentau1991]
- 110.5: Variable region sequenced – heavy chain: V 3660-SB32, D closest to DSP2.3, 2.4 and .6, J H2 – light chain: V kappa21, J kappa2 [Pirofski1993]
- 110.5: Thrombin cleavage of V3 loop between R-315 and A-316 abrogates binding – can inhibit C4 region antibody which has conformational requirements (G3-299) – binding to native gp120 100-300 fold greater than to denatured [Moore1993c]
- 110.5: The gp41 mutation 582(Ala to Thr) results in conformational changes in gp120 that confer neutralization resistance to conformationally sensitive neutralizing MAbs – neutralization efficiency of 110.5 is not affected [Reitz1988, Klasse1993a]
- 110.5: Pretreatment of HX10-infected H9 cells with sCD4 decreases signal from 110.5 at 37 degrees due to dissociation of gp120-gp41 [Sattentau1995c]
- 110.5: Binds with high affinity to monomer and oligomer, rapid association and potent neutralization of lab strains – neutralizes cell-free Hx10 [Sattentau1995b]
- 110.5: Reciprocal binding inhibition with other anti-V3 MAbs – enhances binding of some anti-V2 MAbs – binding enhanced by some CD4 binding site MAbs [Moore1996]
- 110.5: V3 MAbs 9284, BAT123, 110.5, and 110.I could each significantly increase gp120 dissociation from virus, mimicking sCD4, and expose the gp41 epitope for MAb 50-69, in contrast to anti-V2 MAbs [Poignard1996a]
- 110.5: Neutralizes HIV-1 LAI [McDougal1996]
- 110.5: Deletion of the V1V2 regions did not affect anti-V3 Abs ability to bind when compared to intact rec gp120 [Jeffs1996]
- 110.5: Viral binding inhibition by 110.5 was correlated with neutralization (all other neutralizing MAbs tested showed some correlation except 2F5) [Ugolini1997]
- 110.5: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren1998a]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
485	58.2	gp160 (310–317)	gp120 (MN)	HIGPGRAF	L	Vaccine	murine (IgG1κ)

Vaccine *Vector/Type:* peptide *Strain:* MN *HIV component:* V3
Ab type V3 **Donor** Repligen Corp.
References White-Scharf1993, Potts1993, Moore1994b, Seligman1996, Stanfield1999, York2001

- 58.2: Epitope defined by peptide reactivity and changes in affinity with amino acid substitutions – 4/7 primarily isolates were neutralized [White-Scharf1993]
- 58.2: Did not synergistically neutralize MN in combination with MAb F105 – there was synergistic neutralization when combined with sCD4 [Potts1993]
- 58.2: Modest cross-reactivity among B clade gp120s, little outside B clade – core epitope as I-IHIG [Moore1994b]
- 58.2: Competition ELISAs with serial deletions produced longer estimates of epitope length, RIHIGPGRAFY, than Alanine substitution, suggesting significance of non-contact residues [Seligman1996]
- 58.2: The crystal structure of Fab 58.2 bound to V3 loop peptides was obtained – conformational changes in the tip of the V3 loop (GPGR) were observed when different MAbs were bound – 58.2's epitope was defined as KRKRIHIGPGRAFY [Stanfield1999]
- 58.2: 58.2's epitope was noted to be IGPGRAF – Abs against the V3 loop (50.1, 58.2, 59.1, 257-D, 268-D, 447-52D), CD4BS (IgG1b12, 559-64D, F105), CD4i (17b), and to gp41 (2F5, F240) each showed similar binding efficiency to Env derived from related pairs of primary and TCLA lines (primary: 168P and 320SI, and TCLA: 168C and 320SI-C3.3), but the TCLA lines were much more susceptible to neutralization suggesting that the change in TCLA lines that make them more susceptible to NAbs alters some step after binding [York2001]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
486	polyclonal	gp160 (310–318)	gp120	QRGPGRAFV?	L	Vaccine	murine (IgA, IgG1, IgG2a)
	Vaccine *Vector/Type:* peptide Brucella abortus (Ba) conjugate, peptide keyhole limpet hemocyanin (KLH) conjugate, peptide lipopolysaccharide (LPS) conjugate *Strain:* MN *HIV component:* V3 **References** Golding2002a • Internasal (i.n.) immunization with V3-Ba induced mucosal anti-V3 NAbs and IFN-gamma secreting T cells – V3-Ba, V3-KLH and V3-LPS could each induce serum and mucosal IgA and IgG in BALB/c mice – i.n. plus i.p. immunizations gave higher titers than i.n. alone – the response to V3-KLH was mainly restricted to IgG1, and to V3-Ba, IgG2a – class II KO mice (CD4+-deficient) did not respond to V3-KLH, but did respond to V3-Ba, suggesting that V3-Ba may be effective in eliciting Ab responses in HIV-1 infected individuals that have impaired CD4+ T cell function [Golding2002a]					
487	537-D (537)	gp160 (311–315)	gp120 (MN)	IGPGR	L	HIV-1 infection	human (IgG1λ)
	Ab type V3 **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center) **References** Karwowska1992b, Gorny1992, Gorny1993, VanCott1994, Fontenot1995, Zolla-Pazner1999a, Zolla-Pazner1999b, Nyambi2000 • 537-D: Reacts with MN, NY5, CDC4, RF, WM52 and SF2, but does not cross-react with HXB2 [Karwowska1992b] • 537-D: MN type specific neutralization observed – binds SF2, also IGPGR [Gorny1992, Gorny1993] • 537-D: Moderate homologous neutralization, relatively rapid dissociation constant [VanCott1994] • 537-D: Review of clade specificity and anti-V3 HIV-1-Abs [Zolla-Pazner1999a] • 537-D: MAb peptide-reactivity pattern clustered with immunological related MAbs: 1334, 419, 504, 447, 453 and 537 – the core amino acids GP tended to be critical for reactivity in this group [Zolla-Pazner1999b] • 537-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 537-D showed weak reactivity [Nyambi2000]					
488	5020	gp160 (311–316)	gp120 (311–316 BH10)	RGPGRA	no	Vaccine	murine (IgG)
	Vaccine *Vector/Type:* peptide *Strain:* BH10 *HIV component:* V3 **Ab type** V3 **References** Langedijk1991 • 5020: Generation and fine mapping of murine MAbs [Langedijk1991]						
489	RC25	gp160 (311–316)	gp120 (JRFL)	IGPGRA	L		humanized murine
	Ab type V3 **References** Kimura2002 • RC25: RC25 is a humanized MAb that recognizes the epitope IGPGRA – it has strong neutralizing activity against JRFL (R5 virus) and weak against NL4-3 (X4 virus) and is used as a control in a study of NAb activity in patients undergoing HAART [Kimura2002]						
490	5023A (5023, NEA-9205, NEA 9205)	gp160 (311–317)	gp120 (311–317 BH10)	RgPGRAF	L	Vaccine	murine (IgG)
	Vaccine *Vector/Type:* peptide *Strain:* BH10 *HIV component:* V3 **Ab type** V3 **Donor** Paul Durda, Du Pont de Nemours and Co **References** Langedijk1991, D'Souza1991, Back1993, Rovinski1995 • 5023A: Generation and Fine mapping of murine MAbs [Langedijk1991] • 5023A: Called 5023 – Langedijk also has an MAb called 5023B – strong cross-reactive neutralizing MAb [D'Souza1991] • 5023A: Called 5023 – Langedijk also has an MAb called 5023B – gp41 amino acid substitutions 668 (N/S) and 675 (I/M) in gp41 interfere with 5023s neutralization potency, region 662-675 is ELDKWANLWNWFNI [Back1993]						

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 5023A: Called 5023 in this paper – Used to precipitate gp160 in immunoblots in a study examining the feasibility of using unprocessed gp160 glycoprotein as an immunogen [Rovinski1995] • 5023A: Called NEA-9205 – The N306 glycan of the V3 loop makes the tip of the V3 loop inaccessible to this MAb in oligomeric Env, loss of this glycan enhances neutralization sensitivity [Schonning1998]					
491	110.6	gp160 (311–318)	gp120 (BRU)	RGPGRAFV	L (weak)	Vaccine	murine (IgG1λ)
		Vaccine *Vector/Type:* infected-cell lysate *Strain:* BRU *HIV component:* virus **Ab type** V3 **References** Thomas1988, Pirofski1993, Langedijk1992 • 110.6: Variable region sequenced – heavy chain: V J558-146b.1alpha, D closest to DSP16.2, J H3 – light chain: V lambda1, J lambda1 [Pirofski1993]					
492	polyclonal	gp160 (311–318)	gp120 (MN)	IGPGRAFY	L	Vaccine	murine (IgG2a)
		Vaccine *Vector/Type:* B. abortus complex *Strain:* SF2, MN *HIV component:* gp120 **Ab type** V3 **References** Golding1995 • Ab is evoked even in mice depleted of CD4+ cells					
493	10/36e	gp160 (311–321)	gp120 (311–321 HXB10)	RGPGRAFVTIG	L (HXB10)	Vaccine	rat (IgG2a)
		Vaccine *Vector/Type:* recombinant protein *Strain:* BH10 *HIV component:* gp120 **Ab type** V3 **References** McKeating1992a, McKeating1993b, Peet1998 • 10/36e: Binding to virion gp120 enhanced by sCD4 [McKeating1992a] • 10/36e: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind, but anti-V3 MAb 10/36e binding was dramatically diminished by V3 serine substitutions – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions [Peet1998]					
494	10/54 (10/54ow/6i/6i)	gp160 (311–321)	gp120 (311–321 HXB10)	RGPGRAFVTIG	L (HXB10)	Vaccine	rat (IgG1)
		Vaccine *Vector/Type:* recombinant protein *Strain:* BH10 *HIV component:* gp120 **Ab type** V3 **References** McKeating1992a, McKeating1993a, McKeating1993b, Peet1998 • 10/54: Binding to virion gp120 enhanced by sCD4 [McKeating1992a] • 10/54: Studied in the context of a neutralization escape mutant [McKeating1993a] • 10/54: Called 10/54ow/6i/6i: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind, but anti-V3 MAb 10/54 binding was dramatically diminished by V3 serine substitutions – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions [Peet1998]					
495	11/85b (11/85b/14I/14I)	gp160 (311–321)	gp120 (311–321 HXB10)	RGPGRAFVTIG	L (HXB2)	Vaccine	rat (IgG2b)
		Vaccine *Vector/Type:* recombinant protein *Strain:* BH10 *HIV component:* gp120 **Ab type** V3					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References McKeating1992a, McKeating1993b • 11/85b: Binding to virion gp120 enhanced by sCD4 [McKeating1992a]					
496	polyclonal	gp160 (311–322)	gp120 (MN)	IGPGRAFYTTKN	L (MN ALA-1)	Vaccine	guinea pig
		Vaccine *Vector/Type:* human rhinovirus 14 *Strain:* MN *HIV component:* V3 **Ab type** V3 **References** Smith1998 • The tip of the MN V3 loop (IGPGRAFYTTKN) was inserted into cold-causing human rhinovirus 14 (HRV14) – chimeras were immunoselected, and chimeric viruses were neutralized by anti-V3 loop antibodies – chimeric viruses elicited potent NAbs against ALA-1 and MN [Smith1998]					
497	0.5β (0.5 beta, 0.5beta)	gp160 (311–324)	gp120 (316–330 HXB2)	RGPGRAFVTIGKIG	L (IIIB)	Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* protein *Strain:* IIIB *HIV component:* Env **Ab type** V3 **Donor** Shuzo Matsushita or Toshio Hattori of Kumamoto University **References** Matsushita1988, Skinner1988b, Skinner1988a, Reitz1988, Nara1990, D'Souza1991, Matsushita1992, Emini1992, Maeda1992, McKeating1992a, Sperlagh1993, diMarzo Veronese1993, Moore1993c, Klasse1993a, Watkins1993, Cook1994, Thali1994, Okada1994, Boudet1994, Broder1994, Zvi1995b, Zvi1995a, Jagodzinski1996, Warrier1996, McDougal1996, Jeffs1996, Huang1997, Zvi1997, Wyatt1997, Faiman1997, Tugarinov1999, Fortin2000, Jagodzinski2000, Tugarinov2000, Zvi2000 • 0.5beta: Type-specific neutralization of IIIB – does not neutralize MN or RF [Matsushita1988, Skinner1988b] • 0.5beta: Emergence of virus resistant to MAb 0.5beta and autologous sera neutralization in IIIB infected chimps [Nara1990] • 0.5beta: Potent neutralizing activity [D'Souza1991] • 0.5beta: Chimeric mouse-human MAb Cbeta1 was constructed by combining the human Cgamma1 and Ckappa constant regions with the 0.5beta murine MAb – ADCC and neutralizing activity[Matsushita1992] • 0.5beta: sCD4 causes loss of IIIB type-specificity, allowing binding and neutralization of MN, in contrast to MAb mu5.5 [Maeda1992] • 0.5beta: Monoclonal anti-idiotype antibodies that mimic the 0.5beta epitope were generated [Sperlagh1993] • 0.5beta: Neutralization of virus carrying an A to T substitution (contrast with MAb M77) [diMarzo Veronese1993] • 0.5beta: Binding to native gp120 100-300 fold greater than to denatured [Moore1993c] • 0.5beta: The gp41 mutation 582(Ala to Thr) results in conformational changes in gp120 that confer neutralization resistance to some antiserum and conformationally sensitive neutralizing MAbs – neutralization efficiency of 0.5beta is not affected [Reitz1988, Klasse1993a] • 0.5beta: A neutralization escape mutant (HXB2 A281V) was selected by growth of HXB2 in the presence of broadly neutralizing sera – of the MAbs tested , 0.5beta neutralization was the most profoundly affected by this mutation [Watkins1993] • 0.5beta: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – this MAb can inhibit gp120 binding to GalCer in vitro [Cook1994] • 0.5beta: gp41 mutation that confers resistance to neutralization by anti-CD4 binding site antibodies does not reduce neutralizing efficiency of this V3 region MAb [Thali1994] • 0.5beta: Binding domain aa 310-319: RGPGRAFVTIGKIG – mutations in the V3 loop from basic residues can destroy virus infectivity and syncytium formation: R306T, R309T and R313G can also reduce binding of V3 MAbs with two different binding sites: 9284 and 0.5beta [Okada1994] • 0.5beta: Type-specific neutralization of IIIB – does not neutralize SF2 [Broder1994] • 0.5beta: The interactions of the peptide RKSIRIQRGPGRAFVT 0.5beta were studied by NMR, and hydrophobic interactions between the two Is and the V form the base of a 12 amino acid loop with GPGR at the apex[Zvi1995b] • 0.5beta: NMR of 0.5beta bound NNTRKSIRIQRGPGRAFVTIGKIG suggests that the bound amino acids are in the region SIRIQRGPGRAFVT [Zvi1995a]			

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 0.5beta: The sulfated polysaccharide curdlan sulfate (CRDS) binds to the Envelope of T-tropic viruses and neutralizes virus – CRDS inhibits 0.5beta binding – 0.5beta epitope described as GPGRAFVTIG [Jagodzinski1996]
- 0.5beta: Synergistic neutralization of HIV-1 when combined with anti-V2 MAb C108G [Warrier1996]
- 0.5beta: Deletion of the V1V2 regions did not affect anti-V3 Abs ability to bind when compared to intact rec gp120 [Jeffs1996]
- 0.5beta: Relative to the native peptide, an O-linked alpha-galactosamine modified V3 peptide enhanced binding to 0.5 beta, while an N-linked beta-glucosamine modified peptide showed reduced binding [Huang1997]
- 0.5beta: The structure of a 17 amino acid V3 peptide bound to the Fab was studied using NMR [Zvi1997]
- 0.5beta: Binds both gp120 and soluble gp120+gp41 complex efficiently, suggesting its gp120 epitope is not blocked by gp41 binding [Wyatt1997]
- 0.5beta: The Fv fragment was purified and the temperature dependence and effect of mutations was studied [Faiman1997]
- 0.5beta: NMR structure reveals that Ab bound IIIB-V3 peptide adopts an unexpected type VI cis proline beta-turn [Tugarinov1999]
- 0.5beta: Host encoded intercellular adhesion molecule (ICAM-1) is incorporated by the HIV-1 virion and enhances viral infectivity – ICAM-1 does not modify virus sensitivity to antibodies 0.5beta or 4.8D or sCD4, but neutralizing ability of F105 was diminished in ICAM bearing virions in the presence of lymphocyte function-association antigen-1 (LFA-1) Ab [Fortin2000]
- 0.5beta: MAbs 0.5beta and G3-42 were used to study synthesis of oligomeric and monomeric forms of Env – inhibition of glycosylation by tunicamycin results in reduction of oligomeric gp120 at the cell surface and of monomer in the cytoplasm – neither MAb recognized non-glycosylated Env precursor [Jagodzinski2000]
- 0.5beta: 14/18 residues of peptide P1053, RKSIRIQRGPGRAFVTIG, were shown to be involved in the Ab recognition site using NMR – QRGPGR forms a beta-hairpin turn at the center of the binding pocket [Tugarinov2000]
- 0.5beta: NMR and mutation cycles were employed to generate a model of the peptide-antibody complex, showing aa residues that interact or do not contribute to the binding of MAb 0.5beta Fv with the peptide – F96(L) of 0.5beta binds to Pro13, H52(H) interacts with Ile7, Ile9, Gln10, and D56(H) interacts with Arg11 of the V3 loop peptide – RGPG retains hairpin conformation binds in the center of a groove [Zvi2000]
- 0.5beta: UK Medical Research Council AIDS reagent: ARP3025
- 0.5beta: NIH AIDS Research and Reference Reagent Program: 1591

498 | Cβ1, 0.5β | gp160 (311–324) | gp120 (316–330 HXB2) | RGPGRAFVTIGKIG | L | Vaccine | humanized murine (IgG1)

Vaccine *Vector/Type:* protein *Strain:* IIIB *HIV component:* Env
Ab type V3
References Emini1992, Matsushita1992, Kimura2002, Ferrantelli2002

- Cbeta1: passive transfer to chimpanzees confers protection against challenge with homologous cell-free virus – mouse 0.5beta human IgG1 chimera [Emini1992]
- Cbeta1: Chimeric mouse-human MAb Cbeta1 was constructed by combining the human Cgamma1 and Ckappa constant regions with the 0.5beta murine MAb – ADCC and neutralizing activity [Matsushita1992]
- Cbeta1: Defines epitope as IQRGPGRA – strong neutralizing activity against NL4-3 (X4 virus) and none against JRFL (R5 virus) – used as a control in a study of NAb activity in patients undergoing HAART [Kimura2002]
- Cbeta1: Review of passive immunoprophylaxis with human NAbs that also includes this chimeric mouse-human MAb, noting it protected 2/2 Chimpanzees from HIV-1 IIIB infection in the Emini et al study published in 1992 [Ferrantelli2002]

499 | NM-01 | gp160 (312–315) | gp120 (MN) | GPGR | L | Vaccine | murine (IgG)

Vaccine *Vector/Type:* human rhinovirus 14 *Strain:* MN *HIV component:* V3
Ab type V3 **Donor** M. Terada
References Ohno1991, Yoshida1997, Smith1998

- NM-01: Resistance mutation selected by propagation of molecular cloned isolate in the presence of NM-01 [Yoshida1997]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• NM-01: The tip of the MN V3 loop was inserted into cold-causing human rhinovirus 14 (HRV14) – chimeras were immunoselected, and chimeric viruses were neutralized by anti-V3 loop antibodies, and NM-01 was among the Abs used – chimeric viruses elicited potent NAbs in guinea pigs against ALA-1 and MN [Smith1998]					
500	1026	gp160 (312–317)	gp120 (MN)	GPGRAF	L	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* recombinant protein *Strain:* MN *HIV component:* gp120 **Ab type** V3 **References** Nakamura1993, Bou-Habib1994 • 1026: Bound diverse strains, neutralizing activity against MN, close to GPGRAF [Nakamura1993] • 1026: Greater affinity for T cell-tropic strain T-CSF, derived from JR-CSF, than to the primary isolate JR-CSF [Bou-Habib1994]					
501	1034	gp160 (312–317)	gp120 (MN)	GPGRAF	L	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* recombinant protein *Strain:* MN *HIV component:* gp120 **Ab type** V3 **References** Bou-Habib1994, Berman1997 • 1034: Greater affinity for T cell tropic T-CSF, derived from JR-CSF, than to the primary isolate JR-CSF, close to GPGRAF [Bou-Habib1994] • 1034: Binds to 5/7 isolates from breakthrough cases from a MN gp120 vaccine trial [Berman1997]					
502	59.1 (R/V3-59.1)	gp160 (312–317)	gp120 (308–313 MN)	GPGRAF	L	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* peptide *Strain:* MN *HIV component:* V3 **Ab type** V3 **Donor** Mary White-Scharf and A. Profy, Repligen Corporation **References** D'Souza1991, White-Scharf1993, Potts1993, Ghiara1993, Bou-Habib1994, D'Souza1994, Seligman1996, Ghiara1997, Smith1998, Stanfield1999, York2001 • 59.1: Called R/V3-59.1 – potent neutralizing MAb [D'Souza1991] • 59.1: Epitope defined by peptide reactivity and binding affinity with amino acid substitutions – GPGRAF [White-Scharf1993] • 59.1: Synergistic neutralization of MN when combined with sCD4 or the CD4BS MAb F105 [Potts1993] • 59.1: Crystal structure of a 24 amino acid peptide from the V3 loop bound to 59.1 Fab fragment – contact residues IGPGRAF [Ghiara1993] • 59.1: Greater affinity for T-cell tropic strain T-CSF than the primary isolate JR-CSF, from which T-CSF was derived [Bou-Habib1994] • 59.1: Multi-lab study for antibody characterization and assay comparison – neutralizes MN and IIIB [D'Souza1994] • 59.1: Competition ELISAs with serial deletions produced longer estimate of epitope length than x-ray crystallography or Alanine substitution, RIHIGPGRAFYTT, suggesting significance of non-contact residues [Seligman1996] • 59.1: A conformationally restricted analog of the tip of the V3 loop was constructed and bound with Fab 59.1 – crystal structure shows interactions between 59.1 and an MN peptide and 59.1 and the modified peptide are similar, but NMR studies reveal that the modified peptide is more ordered in solution, retaining the Fab bound form [Ghiara1997] • 59.1: The tip of the MN V3 loop was inserted into cold causing human rhinovirus 14 (HRV14) – chimeras were immunoselected, and chimeric viruses were neutralized by anti-V3 loop antibodies, and 59.1 was among the Abs used – chimeric viruses elicited potent NAbs in guinea pigs against ALA-1 and MN [Smith1998] • 59.1: The crystal structure of V3 loop peptides bound to Fabs was obtained – conformational changes in the tip of the V3 loop (GPGR) were observed when different MAbs were bound [Stanfield1999] • 59.1: Abs against the V3 loop (50.1, 58.2, 59.1, 257-D, 268-D, 447-52D), CD4BS (IgG1b12, 559-64D, F105), CD4i (17b), and to gp41 (2F5, F240) each showed similar binding efficiency to Env derived from related pairs of primary and TCLA lines (primary: 168P and 320SI, and TCLA: 168C and 320SI-C3.3), but the TCLA lines were much more susceptible to neutralization suggesting that the change in TCLA lines that make them more susceptible to NAbs alters some step after binding [York2001]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
503	polyclonal	gp160 (312–317)	gp120 (316–321)	GPGRAF		Vaccine	rabbit (Ig)
		Vaccine *Vector/Type:* polyepitope, protein *HIV component:* gp160 *Adjuvant:* BSA **Ab type** V3 **References** Lu2000c, Lu2000b • High titer response to ELDKWA and RILAVERYLKD was observed upon vaccination with multiple-epitope vaccine CG-GPGRAFY-G-ELDKWA-G-RILAVERYLKD conjugated to BSA, a weak response to GPGRAFY – immunization with CG-(ELDKWA-GPGRAFY)_2-K was also tried, yielding a strong Ab response to ELDKWA, weak to GPGRAF – gp160 vaccination yielded strong Ab response but not to any of the peptides studied here [Lu2000c, Lu2000b]				
504	10E3	gp160 (312–318)	gp120 (317–323 IIIB)	GPGRAFY		Vaccine	murine (IgG)
		Vaccine *Vector/Type:* peptide keyhole limpet hemocyanin (KLH) conjugate *Strain:* IIIB *HIV component:* V3 **Ab type** V3 **References** Tian2001 • 10E3: Peptides GPGRAFY and ELDKWAG were conjugated to KLH and used to raise mouse monoclonal Ab – MAb hybridomas were generated with defined specificity – 10E3 binds to the peptide GPGRAFY and to rgp160 [Tian2001]				
505	polyclonal	gp160 (312–318)	gp120 (317–323)	GPGRAFY		Vaccine	murine, rabbit
		Vaccine *Vector/Type:* peptide *HIV component:* V3 *Adjuvant:* BSA **Ab type** V3 **References** Yu2000 • High levels of epitope-specific Abs were induced by the peptide-BSA conjugates C-(GPGRAF)_4-BSA or C-(TRPNNNTRKSIRIQRGPGRAFYTIG KI)-BSA but not by rgp160 vaccine [Yu2000]				
506	N11-20 (110-H)	gp160 (312–320)	gp120 (317–325)	GPGRAFVTI	L (LAI)		murine (IgG1κ)
		Ab type V3 **Donor** J. C. Mazie, Hybridolab, Institut Pasteur **References** Valenzuela1998 • N11-20: Neutralization of LAI in CEM cells by anti-V3 MAbs 110.4 and N11-20 is through inhibition of virus binding to the cell [Valenzuela1998]				
507	5025A (5025)	gp160 (313–317)	gp120 (313–317 BH10)	pgRAF	L	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* peptide *Strain:* BH10 *HIV component:* V3 **Ab type** V3 **Donor** Paul Durda, Du Pont de Nemours and Co **References** Langedijk1991, D'Souza1991 • 5025A: Generation and fine mapping of murine MAbs [Langedijk1991] • 5025: Called 5025 – strain specific weakly neutralizing [D'Souza1991]				
508	N70-1.9b	gp160 (313–318)	gp120 (316–322)	PGRAFY	L	HIV-1 infection	human (IgG1)
		Ab type V3 **References** Robinson1990a, Scott1990 • N70-1.9b: Type specificity [Robinson1990a] • N70-1.9b: Type specific neutralization, ADCC directed against MN infected cells [Scott1990]					
509	902	gp160 (313–324)	gp120 (IIIB)	PGRAFVTIGKIG	L	Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* gp160 **Ab type** V3 **Donor** Bruce Chesebro, Rocky Mountain National Laboratory, Montana					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Chesebro1988, Laman1993, Broder1994, Earl1994, Sakaida1997 • 902: Strain specific neutralization of HIV [Chesebro1988] • 902: Epitope may be partially masked or altered in the oligomeric molecule [Broder1994] • 902: Used as a control in a study of the influence of oligomeric structure of Env in determining the repertoire of the Ab response [Earl1994] • 902: V3-BH10 peptide with loop-structure inhibits IL-2 induced T-cell proliferation, thought to be due to altering intracellular signaling, and MAb 908 can block the peptide inhibition [Sakaida1997] • 902: NIH AIDS Research and Reference Reagent Program: 522					
510	694/98-D (694/98, 694.8, 694/98D)	gp160 (314–317)	gp120 (IIIB)	GRAF	L	HIV-1 infection	human (IgG1λ)
		Ab type V3 **Donor** Drs. S. Zolla-Pazner and M. Gorny, NYU Med Center NY, NY **References** Gorny1991, Gorny1992, Gorny1993, Cavacini1993a, Spear1993, Gorny1994, Laal1994, VanCott1994, Cook1994, VanCott1995, Zolla-Pazner1995a, Forthal1995, Li1997, Zolla-Pazner1997, Smith1998, Li1998, Andrus1998, Nyambi1998, Schonning1998, Zolla-Pazner1999a, Zolla-Pazner1999b, Altmeyer1999, Nyambi2000, Park2000, Edwards2002, He2002, Zhang2002 • 694/98-D: This MAb was first described here [Skinner1988b] • 694/98-D: Type-specific lab isolate neutralization was observed – binds with 1-3 fold greater affinity to gp120 than to peptides [Gorny1992] • 694/98-D: Neutralizes MN and IIIB (GRAF) – binds SF2 (GRAF) – binding reactivity: MN, IIIB, SF2, NY5, RF, CDC4, WM52 [Gorny1993] • 694/98-D: Called 694-D – complement mediated virolysis of IIIB, but not in the presence of sCD4 [Spear1993] • 694/98-D: 50% neutralization of HIV-IIIB at a concentration of 0.15mug/ml [Gorny1994] • 694/98-D: Potent neutralization of IIIB – no neutralization synergy in combination with CD4 binding domain MAbs [Laal1994] • 694/98-D: GRVY did not alter peptide binding – GRVI and GQAW enhanced dissociation – GQVF and GQAL did not bind [VanCott1994] • 694/98-D: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – V3 MAbs can inhibit gp120 binding to GalCer in vitro – binding of GalCer to gp120 inhibited but did not completely block MAb binding[Cook1994] • 694/98-D: Human HIV-1 infected sera and MAb 694/98 have high reactivity to MN and RF infected H9 cells, but Genentech rec gp120 IIIB vaccine recipients do not [VanCott1995] • 694/98-D: Serotyping study using flow-cytometry – bound GRAX bearing virus in 10/11 cases – somewhat conformation dependent [Zolla-Pazner1995a] • 694/98-D: ADCC activity, and no viral enhancing activity [Forthal1995] • 694/98-D: One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB env – could only achieve 50% neutralization alone – all Ab combinations tested showed synergistic neutralization – 694/98-D has synergistic response with MAbs F105, 15e, b12, 2F5, 17b, 2G12, and 48d, and with HIVIG [Li1997] • 694/98-D: Used to study pre- and post-exposure prophylaxis Hu-PBL-SCID mice infected by an intraperitoneal injection of HIV-1 LAI – MAb half-life in plasma in mice is 9 days – 2 hours post-694/98-D mice were challenged with LAI, and at an Ab concentration of 1.32 mg/Kg, 50% of the mice were infected – one of the infected mice carried the resistant form GRTF rather than GRAF (critical amino acids for binding are GRA) – post-exposure prophylaxis was effective if delivered 15 min post-exposure, but declined to 50% if delivered 60 min post-exposure, and similar time constraints have been observed for HIVIG, 2F5 and 2G12, in contrast to MAb BAT123 that could protect delivered 4 hours post infection [Andrus1998] • 694/98-D: The tip of the MN V3 loop was inserted into cold causing human rhinovirus 14 (HRV14) – chimeras were immunoselected, and chimeric viruses were neutralized by anti-V3 loop antibodies, and 694/98-D was among the Abs used – chimeric viruses elicited potent NAbs in guinea pigs against ALA-1 and MN [Smith1998] • 694/98-D: Neutralization synergy was observed when the MAbs 694/98-D (V3), 2F5 (gp41), and 2G12 (gp120 discontinuous) were used in combination, and even greater neutralizing potential was seen with the addition of a fourth MAb, F105 (CD4 BS) [Li1998] • 694/98-D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – 694/98-D bound only to B and D clade virions and had limited cross reactivity [Nyambi1998]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 694/98-D: In a study of the influence of the glycan at position 306 of the V3 loop on MAb recognition, anti-V3 MAbs were found to neutralize an HIV-BRU mutant virus that lacks the V3 loop glycan more efficiently than HIV-BRU [Schonning1998] • 694/98-D: Review of clade specificity and anti-V3 HIV-1-Abs [Zolla-Pazner1999a] • 694/98-D: MAb peptide reactivity pattern clustered with immunological related MAbs: 1108, 386, 268, 311, 257, 694.8 – the amino acids HI tended to be critical for reactivity in this group [Zolla-Pazner1999b] • 694/98-D: A Semliki Forest virus (SFV) expression system carrying BX08 env was used to study the conformation of gp120 – intracytoplasmic gp120 was recognized by the anti-V3 MAbs K24 and F5.5, while gp120 at the plasma membrane was detected only by conformation dependent MAbs 2G12, 670-D and 694/98D and not linear V3 MAbs – expression in rat brain also showed that surface-expressed Env was recognized only by the conformation-dependent antibodies and not by anti-V3 antibodies [Altmeyer1999] • 694/98-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 694/98-D showed intermediate reactivity [Nyambi2000] • 694/98-D: Called 694/98D – six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20-100 fold more efficient at neutralizing the sensitive form – the mutation L544P reduced binding of all MAbs against gp120 by causing conformational changes [Park2000] • 694/98-D: Called 694/98D – Truncation of the gp41 cytoplasmic domain of X4, R5, and X4R5 viruses forces a conformation that more closely resembles the CD4 bound state of the external Envelope, enhancing binding of CD4i MAbs 17b and 48d and of CD4BS MAbs F105, b12, and in most cases of glycosylation site dependent MAb 2G12 and the anti-gp41 MAb 246D – in contrast, binding of the anti-V2 MAb 697D and the anti-V3 MAb 694/98D were not affected – viruses bearing the truncation were more sensitive to neutralization by MAbs 48d, b12, and 2G12 – the anti-C5 MAb 1331A was used to track levels of cell surface expression of the mutated proteins [Edwards2002] • 694/98-D: Called 694 – Transgenic mice carrying human genes allowing production of fully human MAbs were used to rapidly create a panel of anti-HIV gp120 MAb producing hybridomas by immunization with HIV SF162 gp120 – the previously described human MAbs 5145A(CD4BS) , 4117C (plus others, V3) and 697D (and SC258, V2) were used as controls [He2002]				
511	MO101/V3,C4	gp160 (314–323 + 494–503) **Ab type** V3-C4 **References** Ohlin1992	gp120 (dis 314–323)	GRAFVTIGKI+LGVAPTKAKR		in vitro stimulation	human (IgM)
		• MO101: Generated in response to IIIB Env 286-467 upon in vitro stimulation of uninfected-donor lymphocytes – reacts with peptides 314-323 + 494-503 from the V3 and C4 regions [Ohlin1992]					
512	MO101/V3,C4	gp160 (314–323 + 494–503) **Ab type** V3-C5 **References** Ohlin1992	gp120 (314–323)	GRAFVTIGKI+LGVAPTKAKR		in vitro stimulation	human (IgM)
		• MO101: Generated through in vitro stimulation of uninfected-donor lymphocytes with pB1 containing IIIB Env 286-467 – reacts with peptides from the V3 and C4 regions, positions 314-323 + 494-503, peptides GRAFVTIGKI + LGVAPTKAKR [Ohlin1992]					
513	MO101/V3,C4	gp160 (314–323 + 494–503) **Ab type** V3-C5 **References** Ohlin1992	gp120 (494–503)	GRAFVTIGKI+LGVAPTKAKR		in vitro stimulation	human (IgM)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• MO101: Generated through in vitro stimulation of uninfected-donor lymphocytes with pB1 containing IIIB Env 286-467 – reacts with peptides from the V3 and C4 regions, positions 314-323 + 494-503, peptides GRAFVTIGKI + LGVAPTKAKR [Ohlin1992]					
514	9205 (NEA-9205 NEA9205)	gp160 (315–317)	gp120 (IIIB)	RAF(corereactivity)	L	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* peptide *Strain:* IIIB *HIV component:* V3 **Ab type** V3 **Donor** NEN, Boston MA, commercial **References** Durda1990, Trujillo1993, Allaway1993, VanCott1994, Fontenot1995, Schonning1998, Schonning1999, Gram2002 • 9205: Also see MAb called 5023A • 9205: Called NEA-9205, epitope RIQRGPGRAFVTIGK – reacts with three human brain proteins of 35, 55, 110 kd molecular weight – similar to 9284 – RAF is the core reactivity [Trujillo1993] • 9205: Synergy with combinations of CD4-based molecules in inhibition of HIV-1 Env mediated cell fusion [Allaway1993] • 9205: Neutralizes IIIB but not MN – significantly slower dissociation constant for IIIB than MN [VanCott1994] • 9205: Called NEA-9205 – The N306 glycan of the V3 loop makes the tip of the V3 loop inaccessible to this MAb in oligomeric Env, loss of this glycan enhances neutralization sensitivity [Schonning1998] • 9205: Called NEA-9205 – the stoichiometry of MAb neutralization was tested and the data indicated that binding for neutralization was was incremental not all or none, i.e., each envelope oligomer binds a single MAb and each Env oligomer bound reduces the chances of infection – 9205 binds only to Env with a glycosylation site mutation in the V3 loop, A308T [Schonning1999] • 9205: Called NEA9205 – gp120 capture ELISAs with MAbs D7324 (anti-C-term) or 9205 (anti-V3) were compared in a study of orientation of glycosylation sites – CD4 binding could only inhibit deglycosylation when gp120 was bound to the plate by D7324, not by 9205, while Abs from HIV-1 infected people inhibited deglycosylation most effectively when gp120 was caught by 9205 [Gram2002]				
515	110.I	gp160 (316–322)	gp120 (316–322)	AFVTIGK	L	Vaccine	murine
		Vaccine *Vector/Type:* recombinant protein *HIV component:* gp120 **Ab type** V3 **Donor** F. Traincard, Pasteur Institute, France **References** Moore1993c, Moore1994c, Sattentau1995b, Moore1996, Poignard1996a, Wyatt1997, Parren1998a • 110.I: Binds to carboxy-terminal side of the V3 loop – inhibits binding of C4 region MAb G3-299 [Moore1993c] • 110.I: Binds equally well to monomer and oligomer, rapid association and potent neutralization of lab strains [Sattentau1995b] • 110.I: Reciprocal binding inhibition with other anti-V3 and anti-C4 MAbs – and enhances binding of some anti-V2 MAbs – binding enhanced by some anti-CD4 binding site MAbs [Moore1996] • 110.I: Epitope suggested to be RAFVTIGK – V3 MAbs 9284, BAT123, 110.5, and 110.I could each significantly increase gp120 dissociation from virus, mimicking sCD4, and expose the gp41 epitope for MAb 50-69, in contrast to anti-V2 MAbs [Poignard1996a] • 110.I: Binds both gp120 and soluble gp120+gp41 complex efficiently, suggesting its gp120 epitope is not blocked by gp41 binding [Wyatt1997] • 110.I: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren1998a]				
516	anti-HIV-2 polyclonal	gp160 (317–320 + 333–225)	gp120 (dis 315–318 SBL6669 HIV-2)	FHSQ+WCR		Vaccine	guinea pig (IgG)
		Vaccine *Vector/Type:* peptide *Strain:* HIV-2 SBL6669-ISY *HIV component:* V3 **Ab type** HIV-2 V3 **References** Morner1999 • Neutralizing Abs against HIV-2 V3 are produced when peptides spanning two non-contiguous parts of the V3 loop are used for vaccination including amino acids 315-318 near the tip (FHSQ) and 329-331 (WCR) at the C-term Cys [Morner1999]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
517	IIIB-V3-01	gp160 (320–328)	gp120 (IIIB)	IGKIGNMRQ	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* peptide *Strain:* IIIB *HIV component:* V3 **Ab type** V3 **Donor** Jon Laman **References** Laman1993 • IIIB-V3-01: Specific for carboxy-terminal flank of the IIIB V3 loop – epitope is hidden native gp120, exposed on denaturation [Laman1993] • IIIB-V3-01: UK Medical Research Council AIDS reagent: ARP3046 • IIIB-V3-01: NIH AIDS Research and Reference Reagent Program: 1726					
518	D/6D1	gp160 (346–377)	gp120 (351–382 LAI)	ASKLREQFGNNKTIIFKQSSGGDPE-IVTHSFN	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* gp120 **Ab type** V4 **References** Bristow1994 • D/6D1: V4 MAb generated in a study of the humoral immune response to Baculovirus-expressed mis-folded rgp120 and rgp160 [Bristow1994]					
519	4D7/4	gp160 (360–380)	gp120 (361–380 LAI)	IFKQSSGGDPEIVTHSFNCGG		Vaccine	murine (IgG)
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* Env **Ab type** V4 **Donor** S. Ranjbar, NIBSC, UK **References** Moore1994c • 4D7/4: C3 region – the relative affinity for denatured/native gp120 is >10 [Moore1994c] • 4D7/4: UK Medical Research Council AIDS reagent: ARP3051					
520	36.1(ARP 329)	gp160 (361–381)	gp120 (362–381 LAI)	FKQSSGGDPEIVTHSFNCGGE		Vaccine	murine (IgG)
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* Env **Ab type** V4 **References** Thiriart1989, Moore1994c • 36.1: The relative affinity for denatured/native gp120 is >30 – mutations 380 G/F, 381 E/P impair binding [Moore1994c] • 36.1: UK Medical Research Council AIDS reagent: ARP329					
521	C12	gp160 (361–381)	gp120 (362–381 LAI)	FKQSSGGDPEIVTHSFNCGGE		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* gp160 **Ab type** V4 **Donor** George Lewis **References** Moore1993a, Moore1994c, Abacioglu1994, Moore1994d • C12: Bound preferentially to denatured IIIB gp120 [Moore1993a] • C12: The relative affinity for denatured/native gp120 is >30 – mutations 380 G/F, 381 E/P, and 384 Y/E impair binding – also binds GEFFYCNSTQLFNS, gp120(380-393 LAI) [Moore1994c] • C12: C3 region – epitope boundaries mapped by peptide scanning, core FNCGG [Abacioglu1994]					
522	110.D	gp160 (380–393)	gp120 (380–393 LAI)	GEFFYCNSTQLFNS	no	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* Env **Ab type** C3 **Donor** F. Traincard, Pasteur Institute, France **References** Moore1994c, Valenzuela1998					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 110.D: The relative affinity for denatured/native gp120 is >50 [Moore1994c]					
523	B32	gp160 (380–393)	gp120 (380–393 LAI)	GEFFYCNSTQLFNS		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* gp160 **Ab type** C3 **References** Moore1994c, Abacioglu1994 • B32: The relative affinity for denatured/native gp120 is >100 – mutations 380 G/F, 381 G/P, 382 F/L, 384 Y/E, and 386 N/R impair binding [Moore1994c] • B32: C3 region – epitope boundaries mapped by peptide scanning – FFY(core) [Abacioglu1994]					
524	polyclonal (VEI4)	gp160 (391–413)	Env	FNSTWFNSTWSTEGSNNTEGSDT		HIV-1 infection	human
		Ab type V4 **References** Carlos1999 • Antibody response to the epitopes in a vaccine construct (VEI) containing peptides from 5 hypervariable regions of gp120 was detected in the sera of HIV-1 positive subjects, including sera from 6 non-subtype B infections – serum samples from San Francisco, Canada and Puerto Rico cohort showed presence of antibodies against all five VEI hypervariable regions, but most consistently against the V3 region peptide NNNTRKSIRIGPGRAFYTTGDIGNIRQ [Carlos1999]					
525	B15	gp160 (395–400)	gp120 (395–400 BH10)	WFNSTW		Vaccine	murine (IgG2b)
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* gp160 **Ab type** V4 **Donor** George Lewis **References** Moore1993a, Moore1993c, Abacioglu1994 • B15: Bound preferentially to denatured IIIB gp120 [Moore1993a] • B15: Binds native BH10 gp120 with 5 fold less affinity than denatured – does not bind native or denatured MN gp120 [Moore1993c] • B15: V4 region – epitope boundaries mapped by peptide scanning [Abacioglu1994]					
526	B34	gp160 (395–400)	gp120 (395–400 BH10)	WFNSTW		Vaccine	murine (IgG2b)
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* gp160 **Ab type** V4 **References** Abacioglu1994 • B34: V4 region – epitope boundaries mapped by peptide scanning [Abacioglu1994]					
527	7F11	gp160 (397–439)	gp120 (IIIB)			Vaccine	murine
		Vaccine *Vector/Type:* protein *HIV component:* gp120 **References** Lasky1987, Nilsen1996 • 7F11: There is another MAb with this name that binds to integrase [Nilsen1996]					
528	5C2E5	gp160 (422–431)	gp120 (406–415 IIIB)	QFINMWQEVK		Vaccine	murine
		Vaccine *Vector/Type:* protein *HIV component:* gp120 **Ab type** C4 **Donor** T. Gregory and R. Ward, Genentech, San Francisco **References** Lasky1987, Cordell1991 • 5C2E5: Blocks the gp120-CD4 interaction [Lasky1987] • 5C2E5: Cross-competition with MAbs 5C2E5, ICR38.8f and ICR38.1a [Cordell1991]					
529	G3-211	gp160 (423–437)	gp120 (423–437 IIIB)	IINMWQKVGKAMYAP	L	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* virus derived protein *Strain:* IIIB *HIV component:* gp120					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		Ab type C4 **References** Sun1989 • G3-211, 42, 299, 508, 519, 536, 537: Cross-react with diverse strains by immunofluorescence – blocks HIV binding to CD4+ cells – different neutralization efficiencies [Sun1989]					
530	G3-537	gp160 (423–437)	gp120 (423–437 IIIB)	IINMWQKVGKAMYAP	L	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* virus derived protein *Strain:* IIIB *HIV component:* gp120 **Ab type** C4 **References** Sun1989, Ho1991b, McKeating1992b • G3-537, 211, 299, 508, 519, 536, 42: Cross-react with diverse strains by immunofluorescence – blocks HIV binding to CD4+ cells – different neutralization efficiencies [Sun1989] • G3-537: Weakly neutralizing – binds to a linear binding domain of gp120, NMWQEVGKAMYAPPISG [McKeating1992b]					
531	polyclonal	gp160 (425–436)	gp120	NMWQEVGKAMYA	L	Vaccine	murine (IgA)
		Vaccine *Vector/Type:* peptide *Strain:* IIIB *Adjuvant:* cholera toxin adjuvant **Ab type** CD4BS **References** Bukawa1995 • Polyclonal secretory IgA antibody raised by mucosal immunization is able to neutralize IIIB, SF2, and MN – HIV-1 neutralization may be due to the V3, CD4 or HPG30 component of the multicomponent peptide immunogen [Bukawa1995]					
532	1795	gp160 (425–441)	gp120 (425–441 IIIB)	NMWQEVGKAMYAPPISG	L	Vaccine	
		Vaccine *Vector/Type:* poliovirus *HIV component:* Env **Ab type** CD4BS **References** McKeating1992b • 1795: CD4 binding site – weakly neutralizing – binding inhibited by WQEVGKAMYA, GKAM may be involved [McKeating1992b]					
533	ICR38.1a (38.1a, 388/389, ARP388/389)	gp160 (429–438)	gp120 (dis 427–436 BRU)	EVGKAMYAPP	L	Vaccine	rat (IgG2b)
		Vaccine *Vector/Type:* recombinant protein *Strain:* BH10 *HIV component:* gp120 **Ab type** C3, C4 **References** Cordell1991, McKeating1992b, McKeating1992a, McKeating1992c, McKeating1993b, McKeating1993a, Moore1993c, Jeffs1996, Peet1998, Kropelin1998, Vella2002 • ICR38.1a: Weakly neutralizing – binds linear determinant in the CD4 binding domain – cross-competition with MAbs G3-536, 5C2E5, and ICR38.8f [McKeating1992b, Cordell1991] • ICR38.1a: Unable to exert a synergistic effect in combination with V3 directed MAbs, in contrast to MAb 39.13g, that binds to a conformational epitope involved in CD4 binding [McKeating1992a] • ICR38.1a: Studied in the context of a neutralization escape mutant [McKeating1993a] • ICR38.1a: Unreactive with solid-phase decapeptide, competed in solution phase assay – ICR 38.1a and ICR 38.8f were initially reported to be independent MAbs, but are actually subclones of the same MAb [Moore1993c] • ICR38.1a: Called 38.1a – 10 to 20 fold increased binding when V1/V2 or V1/V2 and V3 were deleted from gp120 [Jeffs1996] • ICR38.1a: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind – ICR38.1a was not affected by V3 serine substitutions – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions [Peet1998]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- ICR38.1a: Called 388/389 – anti-C1 region MAb 87-135/9 blocks gp120 interaction with CD4+ cells – blocking activity is additive when combined with antibodies which bind in the C4 region of gp120 (F105, 388/389, and b12) [Kropelin1998]
- ICR38.1a: Called ARP388/ARP389: Herpesvirus saimiri-immortalized CD4+ T lymphocytes (HVS T cells) were used to isolate virus and perform HIV-1 neutralization assays, and compared with a standard PBMC protocol – neutralization sensitivities to a panel of MAbs and to homologous or heterologous plasma/sera were similar for HVS T cells (CN-2 cells) and PBMCs – lists epitope as WQEVGKAMYA [Vella2002]
- ICR38.1a: UK Medical Research Council AIDS reagent: ARP388/ARP389

534 G3-299 gp160 (429–438) gp120 (429–438 BRU) EVGKAMYAPP L Vaccine murine (IgG1)

Vaccine *Vector/Type:* virus derived protein *HIV component:* gp120
Ab type C4 **Donor** M. Fung and Tanox Biosystems Inc and David Ho, ADARC, NY
References Sun1989, Moore1993c, Sattentau1995b, Moore1996, Poignard1996a, Binley1997a, Ditzel1997, Wyatt1997, Parren1998a

- G3-299: Best neutralization of IIIB in panel of 7 MAbs that bind overlapping epitope [Sun1989]
- G3-299: C4 region – binds HXB2 20mer KQIINMWQKVGKAMYAPPIS, and SF-2 and MN gp120s – G3-42, G3-299 lower affinity than G3-508, G3-519, and G3-536 – bound native gp120, not denatured – poor peptide binding, epitope spans V3-C4 regions – 433A/L, 435Y/H and 430V/S substitutions impaired binding, V3 loop cleavage or insertion abolished binding [Moore1993c]
- G3-299: Binds with higher affinity to monomer than to oligomer, slow association rate, although faster than other C4 MAbs tested, with more potent neutralization of lab strain [Sattentau1995b]
- G3-299: Discontinuous V3-C4 epitope, binding enhanced by a few anti-C1, anti-CD4 binding site, and V2 MAbs – binding reciprocally inhibited by anti-V3 MAbs – G3-229 enhances the binding of some anti-V2 MAbs [Moore1996]
- G3-299: Epitope described as KQIINMWQKVGKAMYAPPIS – binding resulted in slight gp120 dissociation from virus and exposure of the gp41 epitope for MAb 50-69 [Poignard1996a]
- G3-299: Binds both gp120 and soluble gp120+gp41 complex efficiently, suggesting its gp120 epitope is not blocked by gp41 binding [Wyatt1997]
- G3-299: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren1998a]

535 G3-42 (G3 42) gp160 (429–438) gp120 (429–438 BRU) EVGKAMYAPP L Vaccine murine (IgG1)

Vaccine *Vector/Type:* virus derived protein *Strain:* IIIB *HIV component:* gp120
Ab type C4 **Donor** Tanox Biosystems Inc and David Ho, ADARC, NY
References Sun1989, Moore1993c, Thali1993, Sattentau1995b, Jagodzinski1996, Moore1996, Poignard1996a, Trkola1996a, Binley1997a, Binley1999, Jagodzinski2000

- G3-42: Neutralization of IIIB but not RF [Sun1989]
- G3-42: C4 region – binds HXB2 20mer KQIINMWQKVGKAMYAPPIS, and SF-2 and MN gp120s – G3-42, G3-299 have lower affinity than G3-508, G3-519, and G3-536 – bound native gp120, not denatured – poor peptide binding, epitope spans V3-C4 regions – 433A/L, 435Y/H and 430V/S substitutions impaired binding, V3 loop insertion abolished binding [Moore1993c]
- G3-42: Inhibits binding of CD4 inducible MAb 48d [Thali1993]
- G3-42: Binds with higher affinity to monomer than to oligomer, slow association rate [Sattentau1995b]
- G3-42: The sulfated polysaccharide curdlan sulfate (CRDS) binds to the Envelope of T-tropic viruses and neutralizes virus – CRDS potently inhibits G3-42 binding – G3-42 epitope described as KVGKAMYAPP [Jagodzinski1996]
- G3-42: Inhibits binding of many anti-V3, -CD4 binding site, and -C4 region MAbs – enhances binding of some anti-V2 region MAbs [Moore1996]
- G3-42: Epitope described as KQIINMWQKVGKAMYAPPIS – binding resulted in slight gp120 dissociation from virus and exposure of the gp41 epitope for MAb 50-69 [Poignard1996a]
- G3-42: Called G3 42 – Does not inhibit gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study – described as V3-C4 discontinuous epitope [Trkola1996a]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• G3-42: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes [Binley1999] • 0.5beta: MAbs 0.5beta and G3-42 were used to study synthesis of oligomeric and monomeric forms of Env – inhibition of glycosylation by tunicamycin results in reduction of oligomeric gp120 at the cell surface and of monomer in the cytoplasm – neither MAb recognized non-glycosylated Env precursor [Jagodzinski2000]					
536	G3-508 (G3 508)	gp160 (429–438)	gp120 (429–438 BRU)	EVGKAMYAPP	L	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* virus derived protein *Strain:* IIIB *HIV component:* gp120 **Ab type** C4 **Donor** M. Fung and Tanox Biosystems Inc and David Ho, ADARC, NY **References** Sun1989, Thali1993, Moore1993c, Sattentau1995b, Moore1996, Poignard1996a, Trkola1996a, Binley1997a, Parren1998a, Binley1998 • G3-508: Neutralization of IIIB and RF [Sun1989] • G3-508: Inhibits binding of CD4 inducible MAb 48d [Thali1993] • G3-508: C4 region – binds HXB2 20mer KQIINMWQKVGKAMYAPPIS, and SF-2 and MN gp120s – bound denatured with 10 fold greater affinity than native – 433A/L, 435Y/H and 430V/S substitutions impaired binding [Moore1993c] • G3-508: Binds with higher affinity to monomer than to oligomer, slow association rate [Sattentau1995b] • G3-508: Inhibits binding of some V3, C4 and CD4 binding site MAbs, enhances binding of V2 region MAbs [Moore1996] • G3-508: Binding resulted in slight gp120 dissociation from virus and exposure of the gp41 epitope for MAb 50-69 [Poignard1996a] • G3-508: Called G3 508 – inhibits gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study [Trkola1996a] • G3-508: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren1998a] • G3-508: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer [Binley1998]					
537	G3-519	gp160 (429–438)	gp120 (429–438 BRU)	EVGKAMYAPP	L	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* virus derived protein *Strain:* IIIB *HIV component:* gp120 **Ab type** C4 **Donor** Tanox Biosystems Inc and David Ho, ADARC, NY **References** Sun1989, Moore1993a, Moore1993c, D'Souza1994, Sattentau1995b, Moore1996, Poignard1996a, Binley1997a, Wyatt1997, Parren1998a, Binley1999 • G3-519: Best neutralization of RF in panel of 7 MAbs that bind overlapping epitope [Sun1989] • G3-519: Neutralizes IIIB, is reactive with SF-2 gp120, mild inhibition of HIV-1+ sera binding to IIIB gp120 [Moore1993a] • G3-519: C4 region – binds HXB2 20mer KQIINMWQKVGKAMYAPPIS, and SF-2 and MN gp120s – bound denatured with 5 fold greater affinity than native – 433A/L, 435Y/H, 438P/R and 430V/S substitutions impaired binding [Moore1993c] • G3-519: Included in a multi-lab study for antibody characterization, and binding and neutralization assay comparison, also binds IIIB: IINMWQKVGKAMYAPP [D'Souza1994] • G3-519: Binds with higher affinity to monomer than to oligomer, slow association rate [Sattentau1995b] • G3-519: Non-reciprocal enhanced binding in the presence of the C5 MAb 1C1 and the C1 MAb 135/9 – reciprocal enhanced binding with some V2 MAbs. Inhibited binding the presence of some C4, V3 and CD4 binding site MAbs [Moore1996]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• G3-519: Epitope described as KVGKAMYAPP – binding resulted in slight gp120 dissociation from virus but no significant exposure of the gp41 epitope for MAb 50-69 [Poignard1996a] • G3-519: Binds both gp120 and soluble gp120+gp41 complex efficiently, suggesting its gp120 epitope is not blocked by gp41 binding [Wyatt1997] • G3-519: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren1998a] • G3-519: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes [Binley1999]			
538	G3-536	gp160 (429–438)	gp120 (429–438 BRU)	EVGKAMYAPP	L	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* virus derived protein *Strain:* IIIB *HIV component:* gp120 **Ab type** C4 **Donor** Tanox Biosystems Inc and David Ho, ADARC, NY **References** Sun1989, Ho1991b, Cordell1991, McKeating1992b, Moore1993a, Moore1993c, Gorny1994, Sattentau1995b, Moore1996, Poignard1996a, Parren1998a • G3-536: Weak neutralization of IIIB and RF – cross-react with diverse strains by immunofluorescence – blocks HIV binding to CD4+ cells – epitope:IINMWQKVGKAMYAP [Sun1989] • G3-536: Cross-competition with MAbs 5C2E5, ICR38.8f and ICR38.1a [Cordell1991] • G3-536: Weakly neutralizing – binds to a linear determinant in the CD4 binding domain of gp120 [McKeating1992b] • G3-536: Neutralizes IIIB, is reactive with SF-2 gp120, mild inhibition of HIV-1+ sera binding to IIIB gp120 [Moore1993a] • G3-536: C4 region – binds HXB2 20mer KQIINMWQKVGKAMYAPPIS, and SF-2 and MN gp120s – bound denatured with 15 fold greater affinity than native – 433A/L, 435Y/H, 438P/R, and 430V/S substitutions impaired binding [Moore1993c] • G3-536: Enhances binding of anti-V2 MAb 697-D [Gorny1994] • G3-536: Binds with higher affinity to monomer than to oligomer, slow association rate [Sattentau1995b] • G3-536: Inhibits binding of some V3, C4 and CD4 binding site MAbs, enhances binding of V2 region MAbs [Moore1996] • G3-536: Epitope described as KVGKAMYAPP [Poignard1996a] • G3-536: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren1998a]			
539	ICR38.8f	gp160 (429–438)	gp120 (429–438 BRU)	EVGKAMYAPP	L	Vaccine	rat (IgG2b)
		Vaccine *Vector/Type:* recombinant protein *Strain:* BH10 *HIV component:* gp120 **Ab type** C4 **References** Cordell1991 • ICR38.8f: Weakly neutralizing – binds linear determinant in the CD4 binding domain – cross-competition with ICR38.1a, 5C2E5, and G3-536 [Cordell1991] • ICR38.8f:ICR 38.1a and ICR 38.8f were initially reported to be independent MAbs, but are actually subclones of the same MAb [Moore1993c]			
540	MO86/C3	gp160 (429–443)	gp120 (429–443)	EVGKAMYAPPISGQI		in vitro stimulation	human (IgM)
		Ab type C4					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Ohlin1992 • MO86: Generated in response to IIIB Env 286-467 upon in vitro stimulation of uninfected-donor lymphocytes [Ohlin1992]					
541	13H8	gp160 (431–440)	gp120 (412–453)	GKAMYAPPIS	L	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* recombinant protein *Strain:* MN **Ab type** C4 **References** Nakamura1992, Nakamura1993, Jeffs1996 • 13H8: Cross blocks 5C2 in IIIB-rsgp160 ELISA – reactive with diverse strains in rgp120 ELISA [Nakamura1992] • 13H8: Bound diverse strains, neutralizing activity against MN [Nakamura1993] • 13H8: Binds V3 and C4 peptides (J. P. Moore, per. comm.) • 13H8: 3 and 4.5 fold increased binding when V1/V2 or V1/V2 and V3 were deleted from gp120, respectively [Jeffs1996]					
542	G45-60	gp160 (431–440)	gp120 (429–438 BRU)	GKAMYAPPIS	L	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* virus derived protein *Strain:* IIIB *HIV component:* gp120 **Ab type** C4 **References** Sun1989, Moore1993c, Gorny1994, Moore1996, Jagodzinski1996 • G45-60: C4 region – binds HXB2 20mer KQIINMWQKVGKAMYAPPI, decapeptide flanking peptides also bound – bound equivalently to native and denatured gp120 – 433A/L and 435Y/H (not 430V/S) substitutions impaired binding [Moore1993c] • G45-60: Enhances binding of anti-V2 MAb 697-D [Gorny1994] • G45-60: Non-reciprocal enhancement of G45-60 binding by some C1 and C5 antibodies – reciprocal enhancement of some V2 region MAbs – reciprocal inhibition with many MAbs that bind to the V3, C4 and CD4 binding site regions [Moore1996] • G45-60: The sulfated polysaccharide curdlan sulfate (CRDS) binds to the Envelope of T-tropic viruses and neutralizes virus CRDS inhibits G45-60 binding [Jagodzinski1996]					
543	polyclonal	gp160 (432–451)	gp120 (42–61 LAI)	KAMYAPPISGQIRCSSNITG	no	Vaccine	murine
		Vaccine *Vector/Type:* vaccinia *HIV component:* Env **Ab type** C4 **References** Collado2000 • Vaccinia p14 can elicit NAbs and p39 tends to be immunodominant, so these two proteins were fused to regions of HIV-1 Env – reduced glycosylation was noted when p14 or p39 was placed in the N-term region of the fusion protein – chimeric proteins shifted the Env Ab response from V3 to either a C1 or C4 domain, depending on the construct – all chimeric Env proteins: 14kEnv, 39kEnv, and Env39k elicited a strong Ab response to the C1 region of gp120 (LFCASDAKAYDTEVHNVWAT), and Env39k mounted a strong response to the C4 region (KAMYAPPISGQIRCSSNITG) [Collado2000]					
544	1662	gp160 (433–439)	gp120 (IIIB)	AMYAPPI	no	Vaccine	
		Vaccine *Vector/Type:* poliovirus *HIV component:* Env **Ab type** C4 **References** McKeating1992b • 1662: Did not bind to native gp120, epitope not exposed [McKeating1992b]					
545	1663	gp160 (433–439)	gp120 (IIIB)	AMYAPPI	no	Vaccine	
		Vaccine *Vector/Type:* poliovirus *HIV component:* Env **Ab type** C4 **References** McKeating1992b • 1663: Did not bind to native gp120, epitope not exposed [McKeating1992b]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
546	1664	gp160 (433–439)	gp120 (IIIB)	AMYAPPI	no	Vaccine	
		Vaccine *Vector/Type:* poliovirus *HIV component:* Env **Ab type** C4 **References** McKeating1992b • 1664: Did not bind to native gp120, epitope not exposed [McKeating1992b]					
547	1697	gp160 (433–439)	gp120 (IIIB)	AMYAPPI	no	Vaccine	
		Vaccine *Vector/Type:* poliovirus *HIV component:* Env **Ab type** C4 **References** McKeating1992b • 1697: Did not bind to native gp120, epitope not exposed [McKeating1992b]					
548	1794	gp160 (433–442)	gp120 (IIIB)	AMYAPPISGQ	no	Vaccine	
		Vaccine *Vector/Type:* poliovirus *HIV component:* Env **Ab type** C4 **References** McKeating1992b • 1794: Did not bind to native gp120, epitope not exposed [McKeating1992b]					
549	1804	gp160 (433–442)	gp120 (IIIB)	AMYAPPISGQ	no	Vaccine	
		Vaccine *Vector/Type:* poliovirus *HIV component:* Env **Ab type** C4 **References** McKeating1992b • 1804: Did not bind to native gp120, epitope not exposed [McKeating1992b]					
550	1807	gp160 (433–442)	gp120 (IIIB)	AMYAPPISGQ	no	Vaccine	
		Vaccine *Vector/Type:* poliovirus *HIV component:* Env **Ab type** C4 **References** McKeating1992b • 1807: Did not bind to native gp120, epitope not exposed [McKeating1992b]					
551	1808	gp160 (433–442)	gp120 (IIIB)	AMYAPPISGQ	no	Vaccine	
		Vaccine *Vector/Type:* poliovirus *HIV component:* Env **Ab type** C4 **References** McKeating1992b • 1808: Did not bind to native gp120, epitope not exposed [McKeating1992b]					
552	polyclonal (VEI5)	gp160 (454–474)	Env	LTRDGGNNNNESEIFRPGGGD		HIV-1 infection	human
		Ab type V1, V2, V3, V4, V5 **References** Carlos1999 • Antibody response to the epitopes in a vaccine construct (VEI) containing peptides from 5 hypervariable regions of gp120 was detected in the sera of HIV-1 positive subjects, including sera from 6 non-subtype B infections – serum samples from San Francisco, Canada and Puerto Rico cohort showed presence of antibodies against all five VEI hypervariable regions, but most consistently against the V3 region peptide NNNTRKSIRIGPGRAFYTTGDIGNIRQ [Carlos1999]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
553	polyclonal	gp160 (460–467)	gp120 (LAI)	NNNNGSEI		HIV-1 infection, Vaccine	human
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* gp160 **Ab type** V5 **References** Loomis-Price1997 • HIV-1+ positive individuals were given a gp160 vaccine as immunotherapy, and this region was the most reactive new epitope as measured by a modified Pepscan technique which improved sensitivity – 4/14 showed vaccine-induced reactivity [Loomis-Price1997]				
554	CRA1(ARP 323) (CRA-1)	gp160 (461–470)	gp120 (451–470 LAI)	SNNESEIFRL	no	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* Env **Ab type** V5-C5 **Donor** M. Page, NIBSC, UK **References** Moore1993a, Moore1994d, Moore1994c, Moore1996, Trkola1996a, Yang2000 • CRA1: Bound preferentially to denatured IIIB and SF2 gp120 [Moore1993a] • CRA1: Some C5 mutations abrogate binding 470 P/L or G, 475 M/S, some C2 mutations enhance binding [Moore1994d] • CRA1: The relative affinity for denatured/native gp120 is 24 – C5 mutations 470 P/L or G, 475 M/S impairs binding to the native gp120 – only mutation 470 P/L impairs binding to denatured [Moore1994c] • CRA1: C5 region linear epitope, binds weakly to nondenatured monomeric gp120 – reciprocal binding inhibition with anti-C5 antibodies 1C1 and M91 – non-reciprocal binding enhancement some C1 and V2 antibodies – non-reciprocal binding inhibition of some CD4 binding site antibodies [Moore1996] • CRA1: Does not neutralize JR-FL nor block gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study [Trkola1996a] • CRA1: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) that preserve and expose some neutralizing epitopes while occluding some non-neutralizing epitopes – CD4BS MAbs (F105 and F91) and CD4i (17b and 48d) recognized gp140-GNC4 as well as gp120 or gp140 – non-neutralizing MAbs C11, A32, 522-149, M90, and #45 bound to the gp140-GNC4 glycoprotein at reduced levels compared to gp120 – MAbs directed at the extreme termini of gp120 C1 (135/9 and 133/290) and C5 (CRA-1 and M91) bound efficiently to gp140-GNC4 [Yang2000] • CRA1: UK Medical Research Council AIDS reagent: ARP323			
555	M91	gp160 (461–470)	gp120 (451–470 LAI)	SNNESEIFRL	no	Vaccine	rat (IgG2a)
		Vaccine *Vector/Type:* protein *HIV component:* Env **Ab type** V5-C5 **Donor** Fulvia di Marzo Veronese **References** diMarzo Veronese1992, Moore1994c, Moore1994d, Moore1996, Ditzel1997, Binley1998, Yang2000 • M91: Immunoblot reactive, RIP negative, but precipitates deglycosylated gp120 – reacts with strains IIIB, 451, MN, RF, and RUTZ [diMarzo Veronese1992] • M91: The relative affinity for denatured/native gp120 is 24 – mutation in position 470 P/L impairs binding [Moore1994c] • M91: 470 P/L impairs binding, but not 475 D/V, in contrast to CRA1 – some C2 mutations can enhance binding [Moore1994d] • M91: C5 region linear epitope, binds weakly to nondenatured monomeric gp120 – M91 binding was enhanced by 1C1, but 1C1 binding was inhibited by M91 – non-reciprocal binding enhancement of C1 and V2 antibodies – non-reciprocal binding inhibition of CD4 binding site antibodies [Moore1996] • M91: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer [Binley1998] • M91: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) that preserve and expose some neutralizing epitopes while occluding some non-neutralizing epitopes – CD4BS MAbs (F105 and F91) and CD4i (17b and 48d) recognized gp140-GNC4 as well as gp120 or gp140 – non-neutralizing MAbs C11, A32, 522-149, M90, and #45 bound to the gp140-GNC4 glycoprotein at reduced levels compared to gp120 – MAbs directed at the extreme termini of gp120 C1 (135/9 and 133/290) and C5 (CRA-1 and M91) bound efficiently to gp140-GNC4 [Yang2000]			

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
556	9201	gp160 (471–482)	gp120 (475–486 LAI)	GGGDMRDNWRSE	no		murine
		Ab type C5 **Donor** Du Pont **References** McDougal1996 • 9201: Does not neutralize LAI [McDougal1996]					
557	1C1	gp160 (471–490)	gp120 (471–490 LAI)	GGGDMRDNWRSELYKYKVVK		Vaccine	murine (IgG)
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* Env **Ab type** C5 **Donor** Repligen Inc, Cambridge, MA, commercial **References** Moore1994c, Moore1994d, VanCott1995, Moore1996 • 1C1: The relative affinity for denatured/native gp120 is 15 [Moore1994c] • 1C1: C2 and V3 regions substitutions can influence binding [Moore1994d] • 1C1: Linear epitope not exposed on conformationally intact gp120 [VanCott1995] • 1C1: C5 region linear epitope, binds weakly to nondenatured monomeric gp120 – M91 binding was enhanced by 1C1, but 1C1 binding was inhibited by M91 – non-reciprocal binding enhancement of some C1 and V2 antibodies – non-reciprocal binding inhibition of some CD4 binding site antibodies [Moore1996]				
558	3F5	gp160 (471–490)	gp120 (471–490 LAI)	GGGDMRDNWRSELYKYKVVK		Vaccine	murine (IgG)
		Vaccine *Strain:* LAI *HIV component:* Env **Ab type** C5 **Donor** S. Nigida, NCI, USA **References** Moore1994c • 3F5: The relative affinity for denatured/native gp120 is 100 [Moore1994c]					
559	5F4/1	gp160 (471–490)	gp120 (471–490 LAI)	GGGDMRDNWRSELYKYKVVK		Vaccine	murine
		Vaccine *Vector/Type:* peptide *Strain:* HIV-2 ROD **Ab type** C5 **Donor** S. Ranjbar, NIBSC, UK **References** Moore1994c • 5F4/1: V5-C5 region – preferentially binds SDS-DTT denatured gp120 (>10 fold) – mutation 485 K/V impairs binding [Moore1994c]					
560	660-178	gp160 (471–490)	gp120 (471–490 LAI)	GGGDMRDNWRSELYKYKVVK		Vaccine	murine (IgG)
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* Env **Ab type** C5 **Donor** G. Robey, Abbott Labs **References** Moore1994c, Moore1994d • 660-178: The relative affinity for denatured/native gp120 is >100 [Moore1994c] • 660-178: DeltaV1/V2 and DeltaV1/V2/V3 reduce binding – C2 and C5 mutations enhance binding [Moore1994d]					
561	9301	gp160 (471–490)	gp120 (471–490 LAI)	GGGDMRDNWRSELYKYKVVK		Vaccine	murine (IgG)
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* Env **Ab type** C5 **Donor** Dupont, commercial **References** Skinner1988b, Moore1993a, Moore1994c, Moore1994d, Wagner1996 • 9301: Bound preferentially to denatured IIIB gp120 [Moore1993a] • 9301: The relative affinity for denatured/native gp120 is 19 [Moore1994d] • 9301: Wagner et al. claim that Nea 9301 is anti-V3 – might they have meant MAb 9305? [Wagner1996]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
562	B221 (221)	gp160 (471–490)	gp120 (471–490 LAI)	GGGDMRDNWRSELYKYKVVK		Vaccine	murine (IgG1κ)

Vaccine *Vector/Type:* recombinant protein *Strain:* NL43 *HIV component:* gp160
Ab type C5 **Donor** Rod Daniels
References Moore1993a, Bristow1994, Moore1994c

- B221: Called 221 – bound preferentially to denatured IIIB gp120 [Moore1993a]
- B221: MAb generated in a study of the humoral immune response to Baculovirus-expressed mis-folded rgp160 IIIB:NL43, MicroGenSys [Bristow1994]
- B221: The relative affinity for denatured/native gp120 is 12 – mutation 477 D/V impairs binding [Moore1994c]
- B221: Called 221 – C2 and V3 substitutions influence binding [Moore1994d]
- B221: UK Medical Research Council AIDS reagent: ARP301

563	8C6/1	gp160 (471–490)	gp120 (471–490 LAI)	GGGDMRDNWRSELYKYKVVK		Vaccine	murine (IgG)

Vaccine *Strain:* LAI
Ab type V5-C5 **Donor** S. Ranjbar, NIBSC, UK
References Moore1994c

- 8C6/1: V5-C5 region – preferentially binds SDS-DTT denatured gp120 (>30 fold) – mutation 485 K/V impairs binding [Moore1994c]
- 8C6/1: UK Medical Research Council AIDS reagent: ARP3052

564	H11	gp160 (472–477)	gp120 (472–477 HXB2)	GGDMRD			murine

Ab type C5
References Pincus1993a, Pincus1996

- H11: Binds to gp120 but not to infected cells – when linked to ricin A, the immunotoxin did not mediate cell killing – sCD4 has no effect [Pincus1993a, Pincus1996]

565	W2	gp160 (472–491)	gp120 (472–491 LAI)	GGDMRDNWRSELYKYKVVKI		Vaccine	murine (IgG)

Vaccine *Strain:* LAI *HIV component:* Env
Ab type C5 **Donor** D. Weiner, U. Penn., USA
References Moore1994c

- W2: The relative affinity for denatured/native gp120 is 30 – mutation 485 K/V impairs binding [Moore1994c]

566	M38	gp160 (485–504)	gp120 (490–508)	KYKVVKEIPLGVAPTKAKRR	no	Vaccine	murine

Vaccine *Vector/Type:* virus *Strain:* IIIB *HIV component:* virus
Ab type C5
References Beretta1987, Grassi1991, Lopalco1993, DeSantis1994, Beretta1994, Maksiutov2002

- M38: Binds to gp120 and to a 80 kd human protein expressed on a small fraction of mononuclear cells in the lymph nodes [Beretta1987]
- M38: Binds to the carboxy terminus of gp120, in a gp41 binding region, and also to denatured human HLAs (antigenic homology) [Lopalco1993]
- M38: Infected individuals have HLA class I-gp120 cross-reactive antibodies [DeSantis1994]
- M38: This epitope is similar to a fragment of the human protein mast/stem cell growth factor receptor precursor, VVPTKADKRRSV, as well as to a fragment of IFN-related IFRD2 (PC4-B) protein, ARTKARSRVRDKRA [Maksiutov2002].

567	Chim 1 (C-1)	gp160 (487–493)	gp120 (492–498 HXB2)	KVVKEIP			humanized chimpanzee

References Pincus1993a, Pincus1996

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• Chim 1: Binds to gp120 but not to infected cells – when linked to ricin A, the immunotoxin did not mediate cell killing – sCD4 has no effect [Pincus1993a, Pincus1996]					
568	polyclonal	gp160 (489–511)	gp120 (495–516 BRU)	KIEPLGVAPTKAKRRVVQREKR	no	HIV-1 infection	human
		References Hernandez2000, Maksiutov2002 • Chimeric peptide combining two peptides gp160(495-516 and 584-612) served as a specific and broadly reactive antigen for diagnostic detection of HIV-1 [Hernandez2000] • This epitope is similar to a fragment of the human protein mast/stem cell growth factor receptor precursor, VVPTKADKRRSV, as well as to a fragment of IFN-related IFRD2 (PC4-B) protein, ARTKARSRVRDKRA [Maksiutov2002].					
569	1331A	gp160 (490–511)	gp120 (510–516)	dwVVQREKR		HIV-1 infection	human (IgG3λ)
		Ab type C5 **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center) **References** Nyambi1998, Gorny2000a, Hochleitner2000b, Nyambi2000, Gorny2002, Edwards2002 • 1331A: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – anti-C5 Abs 670-D and 1331A bound to 3/4 B clade viruses (they don't bind to IIIB), and to subtype D MAL [Nyambi1998] • 1331A: Core epitope dwVVQREKR maps to gp120(510-516) – binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – C5 MAbs 858-D, 989-D and 1331A bound with a 5-10 fold preference for the monomer[Gorny2000a] • 1331A: The Ab binding site was studied with epitope excision (protein is bound in native conformation to immobilized MAb, then digested with proteolytic enzymes) and extraction (protein is digested then allowed to react with Ab), followed by mass spectroscopy – two non-contiguous aa in C5 were protected, E-507 and I-487, which are thought to be located on opposite sides of hydrophobic pocket involved in gp120/gp41 interaction [Hochleitner2000b] • 1331A: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 4 C5 MAbs, 2 bound well, 2 bound weakly – MAb 858-D bound only 4/26, the worst of all anti-C5 MAbs tested, while MAb 1331A, which shares the same core epitope (positions 495-516), bound to 18/26 [Nyambi2000] • 1331A: Conformation-dependent anti-V3 loop Abs may be more cross-reactive, so six new V3 MAbs were generated – the six new MAbs all bind to the tip of the V3 loop and cross-compete with the MAb 447-52D and are conformationally sensitive – MAbs showed cross-clade binding to native, intact virions and the strength binding was highly correlated with percent neutralization using the ghost cell or PHA blast assay – five well-characterized MAbs were used as controls: anti-V3 447-52D (anti-V3 MAb for competition and neutralization studies), 654 (anti-CD4BS used as a conformation-sensitive MAb control), 1331A (anti-C5 used as a linear binding site MAb control as binding was not diminished by treating gp120 with DTT or sodium metaperiodate to reduce disulfide bonds), and MAb 246 (anti-gp41 MAb that bound to primary isolates of all clades) [Gorny2002] • 1331A: Truncation of the gp41 cytoplasmic domain of X4, R5, and X4R5 viruses forces a conformation that more closely resembles the CD4 bound state of the external Envelope, enhancing binding of CD4i MAbs 17b and 48d and of CD4BS MAbs F105, b12, and in most cases of glycosylation site dependent MAb 2G12 and the anti-gp41 MAb 246D – in contrast, binding of the anti-V2 MAb 697D and the anti-V3 MAb 694/98D were not affected – viruses bearing the truncation were more sensitive to neutralization by MAbs 48d, b12, and 2G12 – the anti-C5 MAb 1331A was used to track levels of cell surface expression of the mutated proteins [Edwards2002]					
570	110.1	gp160 (491–500)	gp120 (491–500 LAI)	IEPLGVAPTK	no	Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* infected-cell lysate *Strain:* BRU *HIV component:* virus **Ab type** C5 **Donor** Genetic Systems Corp, Seattle WA, E. Kinney-Thomas **References** Gosting1987, Linsley1988, Thomas1988, Pincus1991, Moore1994c, Cook1994, McDougal1996, Binley1997a, Valenzuela1998, Maksiutov2002 • 110.1: There is another antibody with this ID that binds to gp120, but at aa 200-217 [Pincus1996] • 110.1: Referred to as 110-1 – does not inhibit CD4-gp120 binding or neutralize HIV-1 strains [Linsley1988]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 110.1: Difference in the epitope: mapped to aa 421-429 (KQIINMWQE), the T1 sequence – poor efficacy as an immunotoxin when linked to RAC [Pincus1991] • 110.1: The relative affinity for denatured/native gp120 is 0.7 [Moore1994c] • 110.1: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – MAbs against the carboxy-terminus of gp120 inhibit gp120 binding to GalCer but not as potently as anti-V3 MAbs – binding of GalCer to gp120 does not inhibit MAb binding [Cook1994] • 110.1: Does not neutralize HIV-1 LAI [McDougal1996] • 110.1: Does effect LAI viral binding or entry into CEM cells [Valenzuela1998] • 110.1: This epitope is similar to a fragment of the human protein mast/stem cell growth factor receptor precursor, VVPTKADKRRSV [Maksiutov2002]					
571	42F	gp160 (491–500)	gp120 (491–500 HXB2)	IEPLGVAPTK	no	HIV-1 infection	human (IgG1λ)
		Ab type C5 **References** Alsmadi1997, Alsmadi1998, Maksiutov2002 • 42F: 42F and 43F were isolated from a long term non-progressor by EBV transformation of PBMC – samples were taken 14 months apart – both MAbs stained diverse strains of infected cells and directed ADCC – were more potent for ADCC if the cell was infected with HIV-1, rather than just presenting absorbed gp120 [Alsmadi1997] • 42F: A study of 6 anti-Env MAbs and their ability to bind or direct ADCC against target cells infected with IIIB, MN, SF-2, and RF – bound and directed lysis against strains IIIB, MN, SF-2, and RF, but not a clone of MN [Alsmadi1998] • 42F: This epitope is similar to a fragment of the human protein mast/stem cell growth factor receptor precursor, VVPTKADKRRSV [Maksiutov2002].					
572	43F	gp160 (491–500)	gp120 (491–500 HXB2)	IEPLGVAPTK	no	HIV-1 infection	human (IgG1λ)
		Ab type C5 **References** Alsmadi1997, Maksiutov2002 • 43F: 42F and 43F were isolated from a long term non-progressor by EBV transformation of PBMC – samples were taken 14 months apart – both MAbs stained diverse strains of infected cells and directed ADCC – were more potent for ADCC if the cell was infected with HIV-1, rather than just presenting absorbed gp120 [Alsmadi1997] • 43F: This epitope is similar to a fragment of the human protein mast/stem cell growth factor receptor precursor, VVPTKADKRRSV [Maksiutov2002].					
573	RV110026	gp160 (491–500)	gp120 (491–500 LAI)	IEPLGVAPTK		Vaccine	human
		Vaccine *Vector/Type:* peptide *Strain:* LAI **Ab type** C5 **Donor** Commercial, Olympus Inc **References** Moore1994c, Moore1994d, Maksiutov2002 • RV110026: Preferentially binds SDS-DTT denatured gp120 (15 fold using R1/87 as capture reagent) [Moore1994c] • RV110026: This epitope is similar to a fragment of the human protein mast/stem cell growth factor receptor precursor, VVPTKADKRRSV [Maksiutov2002].					
574	105-306	gp160 (492–500)	gp120 (498–505 HAM112, O group)	KPFSVAPTP		Vaccine	murine (IgG1 κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* HAM112 (group O) *HIV component:* gp160 **Ab type** C-term **References** Scheffel1999 • 105-306: Overlapping peptides based on group O HAM112 Env were tested for MAb reactivity – 105-306 bound to two overlapping peptides [Scheffel1999]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
575	GV1G2	gp160 (494–499)	gp120 (494–499 IIIB)	LGVAPT		Vaccine	murine

Vaccine *Vector/Type:* protein-Ab complex *HIV component:* gp120 complexed with MAb M77
Ab type C5
References Denisova1996

- GV1G2: When anti-V3 MAb M77 was bound to gp120 and used as an immunogen, it stimulated many MAbs to linear epitopes – MAbs GV12F6 and GV3H1 are homologous to GV1G2 and were generated in the same experiment [Denisova1996]

576	750-D	gp160 (498–504)	gp120 (503–509)	PTKAKRR	no	HIV-1 infection	human (IgG3λ)

Ab type C-term
References Forthal1995, Hioe2000

- 750-D: Not neutralizing, positive ADCC activity, and no viral enhancing activity [Forthal1995]
- 750-D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – CD4BS MAbs or serum Ig from HIV+ individuals inhibited proliferative responses of gp120 specific T cells – C5 MAbs 450-D and 750-D did not effect proliferation [Hioe2000]

577	450-D (450-D-3, 450D)	gp160 (498–504)	gp120 (475–486 BH10)	PTKAKRR(orRRVVQRE,orMRDNW-RSELYKYdependingonreferen-ce)	no	HIV-1 infection	human (IgG1λ)

Ab type C5 **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU Med Center, NY, NY
References Durda1988, Karwowska1992a, Karwowska1992b, Spear1993, Laal1994, Gorny1994, Cook1994, Forthal1995, Manca1995a, Li1997, Hioe1997b, Hioe2000, Hioe2001, Verrier2001

- 450-D: Bound to MN, SF-2 and IIIB, but was not neutralizing [Karwowska1992a]
- 450-D: Did not mediate deposition of complement component C3 on HIV infected cells [Spear1993]
- 450-D: Not neutralizing alone, could synergize anti-CD4 binding site antibody neutralization [Laal1994]
- 450-D: Epitope is defined as PTKAKRR [Gorny1994]
- 450-D: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – MAbs against the carboxy-terminus of gp120 do not inhibit gp120 binding to GalCer – binding of GalCer to gp120 does not inhibit MAb binding [Cook1994]
- 450-D: No neutralizing activity, no ADCC activity, and no viral enhancing activity [Forthal1995]
- 450-D: Virions complexed to gp120 Ab facilitate presentation of p66 RT epitopes to Th cells [Manca1995a]
- 450-D: One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB env – 50% neutralization could not be achieved at a maximal concentration of 6 mug/ml [Li1997]
- 450-D: Four primary isolates showed distinct patterns of sensitivity to neutralization by polyclonal sera or plasma and MAbs – BZ167 was the only isolate inhibited by all polyclonal sera and plasma tested, and was also neutralized by 8/17 MAbs, in particular anti-V3 loop (419-D, 447-52D, 782-D, and 838-D), anti-CD4bd (559/64-D, 654-D and 830-D and a cluster II of gp41 directed MAb (98-6) – isolates 92HT593 and 91US056 were neutralized by V3 loop (419-D, and 447-52D)and cluster II gp41 (98-6) MAbs at higher concentrations – US4 was neutralized by some of the polyclonal sera/plasma tested and not at all by MAbs individually or by a cocktail of ten MAbs consisting of 419-D, 447-52D, 782-D, 838-D, 559/64-D, 654-D, 450-D, 670-D, 1281-D and 98-6 [Hioe1997b]
- 450-D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – CD4BS MAbs or serum Ig from HIV+ individuals inhibited proliferative responses of gp120 specific T cells – C5 MAbs 450-D and 750-D did not effect proliferation [Hioe2000]
- 450-D: CD4BS MAbs when complexed with gp120, inhibit proliferation of gp120-specific CD4 T-cells and IFN gamma production – 450-D does not have this effect and was used as a control in this study [Hioe2001]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 450-D: A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6 – six gave significant neutralization at 2 to 10 ug/ml: 2F5, 50-69, IgG1b12, 447-52D, 2G12, and 670-D six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98-6, and 1281 – no synergy, only additive effects were seen for pairwise combinations of MAbs, and antagonism was noted between gp41 MAbs 50-69 and 98-6, as well as 98-6 and 2F5 [Verrier2001]					
578	670-D (670)	gp160 (498–504)	gp120 (503–509)	PTKAKRR	no	HIV-1 infection	human (IgG1λ)
		Ab type C5 **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU, NY **References** Zolla-Pazner1995a, Forthal1995, Hill1997, Gorny1997, Hioe1997b, Gorny1998, Nyambi1998, Altmeyer1999, Gorny2000b, Nyambi2000, Verrier2001 • 670-D: Group specific cross-clade binding in serotyping study using flow-cytometry [Zolla-Pazner1995a] • 670-D: Not neutralizing, positive ADCC activity, and no viral enhancing activity, numbering provided suggests epitope is RRVVQRE [Forthal1995] • 670-D: gp120 can inhibit MIP-1alpha from binding to CCR5, but this inhibitory effect is blocked by pre-incubation of gp120 with three anti-V3 MAbs: 447, 257, 1027 – MAb 670 which binds in the C5 region had no effect [Hill1997] • 670-D: Four primary isolates showed distinct patterns of sensitivity to neutralization by polyclonal sera or plasma and MAbs – BZ167 was the only isolate inhibited by all polyclonal sera and plasma tested, and was also neutralized by 8/17 MAbs, in particular anti-V3 loop (419-D, 447-52D, 782-D, and 838-D), anti-CD4bd (559/64-D, 654-D and 830-D and a cluster II of gp41 directed MAb (98-6) – isolates 92HT593 and 91US056 were neutralized by V3 loop (419-D, and 447-52D)and cluster II gp41 (98-6) MAbs at higher concentrations – US4 was neutralized by some of the polyclonal sera/plasma tested and not at all by MAbs individually or by a cocktail of ten MAbs consisting of 419-D, 447-52D, 782-D, 838-D, 559/64-D, 654-D, 450-D, 670-D, 1281-D and 98-6 [Hioe1997b] • 670-D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – anti-C5 Abs 670-D and 1331A bound to 3/4 B clade viruses (they didn't bind to IIIB), and to subtype D MAL – 670-D also reacted with subtype A[Nyambi1998] • 670-D: A Semliki Forest virus (SFV) expression system carrying BX08 env was used to study the conformation of gp120 – intracytoplasmic gp120 was recognized by the anti-V3 MAbs K24 and F5.5, while gp120 at the plasma membrane was detected only by conformation dependent MAbs 2G12, 670-D and 694/98D and not V3 MAbs – expression in rat brain also showed that surface-expressed Env was recognized only by the conformation-dependent antibodies and not by anti-V3 antibodies [Altmeyer1999] • 670-D: A gp120 C5 MAb used as a negative control in a study of anti-gp41 MAbs [Gorny2000b] • 670-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 4 C5 MAbs, 2 bound well, 2 bound weakly – MAb 670-D bound 21/26, and was the most cross-reactive C5 MAb [Nyambi2000] • 670-D: A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6 – six gave significant neutralization at 2 to 10 ug/ml: 2F5, 50-69, IgG1b12, 447-52D, 2G12, and 670-D six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98-6, and 1281 – no synergy, only additive effects were seen for pairwise combinations of MAbs, and antagonism was noted between gp41 MAbs 50-69 and 98-6, as well as 98-6 and 2F5 [Verrier2001]					
579	polyclonal	gp160 (503–509)	gp120 (471–477)	RRVVQRE		Vaccine	murine (IgG)
		Vaccine *Vector/Type:* peptide *HIV component:* gp120 **References** Jeyarajah1998 • Mice were immunized with peptide APTKAKRRVVQREKR – epitope excision and extraction combined with mass spectrometry was used to map the fine structure of epitopes recognized by polyclonal Ab to HIV-1 Env – a major epitope was identified between positions 472 and 478 [Jeyarajah1998]					
580	722-D	gp160 (503–509)	gp120 (503–509)	RRVVQRE	no	HIV-1 infection	human (IgG1κ)
		Ab type C-term **References** Laal1994, Forthal1995					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 722-D: Not neutralizing alone, could synergize anti-CD4 binding site antibody neutralization [Laal1994] • 722-D: No neutralizing activity, no ADCC activity, and no viral enhancing activity [Forthal1995]					
581	polyclonal	gp160 (503–511) **Ab type** C-term **References** Palker1987, Loomis-Price1997 • Most HIV-1+ individuals have an antibody response to this epitope – in this study, reactivity to RRVVQREKR was used as a positive control for HIV-1+ gp160 vaccine recipients [Loomis-Price1997]	gp120 (508–516)	RRVVQREKR		HIV-1 infection	human
582	1131-A	gp160 (505–511) **Ab type** C-term **References** Bandres1998 • 1131-A: A very high affinity antibody used in studies that demonstrate that CXCR4 can bind to gp120 in the absence of CD4-gp120 interactions, and that this binding can be enhanced by Env deglycosylation [Bandres1998]	gp120 (510–516 LAI)	VVQREKR	no	HIV-1 infection	human (IgG3λ)
583	858-D	gp160 (505–511) **Ab type** C-term **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center) **References** Zolla-Pazner1995a, Forthal1995, Gorny2000a, Nyambi2000 • 858-D: Group specific cross-clade binding in serotyping study using flow-cytometry [Zolla-Pazner1995a] • 858-D: No neutralizing activity, no ADCC activity, and no viral enhancing activity [Forthal1995] • 858-D: Binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – C5 MAbs 858-D, 989-D and 1331A bound with a 5-10 fold preference for the monomer[Gorny2000a] • 858-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 4 C5 MAbs, 2 bound well, 2 bound weakly – MAb 858-D bound only 4/26, the worst of all anti-C5 MAbs tested, while MAb 1331A, which shares the same core epitope (positions 495-516), bound to 18/26 isolates [Nyambi2000].	gp120 (510–516 LAI)	VVQREKR	no	HIV-1 infection	human (IgG)
584	989-D	gp160 (505–511) **Ab type** C-term **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center) **References** Zolla-Pazner1995a, Gorny2000a, Nyambi2000 • 989-D: In serotyping study using flow-cytometry, showed B clade specificity, but only reacted with 7/11 B clade virus [Zolla-Pazner1995a] • 989-D: Binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – C5 MAbs 858-D, 989-D and 1331A bound with a 5-10 fold preference for the monomer[Gorny2000a] • 989-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 4 C5 MAbs, 2 bound well, 2 bound weakly – MAb 989-D bound to 6/26 isolates [Nyambi2000].	gp120 (LAI)	VVQREKR		HIV-1 infection	human (IgG)
585	1A1	gp160 (525–543) **Donor** H. Katinger, Inst. Appl. Microbiol., Vienna, Austria **References** Buchacher1994, Maksiutov2002 • 1A1: Human MAb generated using EBV transformation of PBL from HIV-1+ volunteers [Buchacher1994] • 1A1: This epitope is similar to a fragment of the HLA class II histocompatibility antigen, GGSCMAALTVTLTV [Maksiutov2002]	gp41 (526–543 BH10)	AAGSTMGAASMTLTVQARQ	no	HIV-1 infection	human (IgG1κ)
586	24G3	gp160 (525–543) **Donor** H. Katinger, Inst. Appl. Microbiol., Vienna, Austria	gp41 (526–543 BH10)	AAGSTMGAASMTLTVQARQ	no	HIV-1 infection	human (IgG1κ)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Buchacher1992, Buchacher1994, Maksiutov2002 • 24G3: Human MAb generated by electrofusion of PBL from HIV-1+ volunteers with CB-F7 cells [Buchacher1994] • 24G3: This epitope is similar to a fragment of the HLA class II histocompatibility antigen, GGSCMAALTVTLTV [Maksiutov2002]					
587	25C2 (IAM 41-25C2)	gp160 (525–543)	gp41 (526–543 BH10)	AAGSTMGAASMTLTVQARQ	no	HIV-1 infection	human (IgG1κ)
		Donor H. Katinger, Inst. Appl. Microbiol., Vienna, Austria and Viral Testing Systems, Houston, TX **References** Buchacher1992, Buchacher1994, Sattentau1995c, Maksiutov2002 • 25C2: Human MAb generated by electrofusion of PBL from HIV-1+ volunteers with CB-F7 cells – binds oligomeric and monomeric gp41, and gp160 [Buchacher1994] • 25C2: Called IAM 41-25C2 – Binding domain overlaps sites that are critical for gp120-gp41 association – binding is enhanced by sCD4 – binding region defined as: gp41(21-38 BH10) [Sattentau1995c] • 25C2: This epitope is similar to a fragment of the HLA class II histocompatibility antigen, GGSCMAALTVTLTV [Maksiutov2002]					
588	5F3	gp160 (525–543)	gp41 (526–543 BH10)	AAGSTMGAASMTLTVQARQ	no	HIV-1 infection	human (IgG1κ)
		Donor H. Katinger, Inst. Appl. Microbiol., Vienna, Austria **References** Buchacher1994, Maksiutov2002 • 5F3: Human MAb generated by electrofusion of PBL from HIV-1+ volunteers with CB-F7 cells [Buchacher1994] • 5F3: This epitope is similar to a fragment of the HLA class II histocompatibility antigen, GGSCMAALTVTLTV [Maksiutov2002]					
589	α(566-586)	gp160 (561–581)	gp41 (566–586 BRU)	AQQHLLQLTVWGIKQLQARIL		HIV-1 infection	human
		References Poumbourios1992					
590	PC5009	gp160 (572–591)	gp41 (577–596 BRU)	GIKQLQARILAVERYLKDQQ		Vaccine	murine
		Vaccine *Vector/Type:* recombinant protein *HIV component:* gp160 **References** Poumbourios1992 • PC5009: Recognized only monomeric gp41 [Poumbourios1992]					
591	polyclonal α577-596	gp160 (572–591)	gp41 (577–596 BRU)	GIKQLQARILAVERYLKDQQ		HIV-1 infection	human
		References Poumbourios1992 • alpha(577-596): Affinity purified from HIV-1+ plasma – preferentially bind oligomer [Poumbourios1992]					
592	polyclonal	gp160 (576–592)	gp41 (583–599)	LQARILAVERYLKDQQL		HIV-1 infection	human
		References Klasse1993b • 42 HIV-1 positive human sera were tested against wildtype peptide, and peptide with substitution 589 A to T: 11/42 reacted strongly with wildtype, weakly with A589T – 31 reacted weakly with parental, even more weakly with substituted [Klasse1993b]					
593		gp160 (577–583)	gp41 (582–589)	QARILAV	yes	HIV-1 exposed seronegative	human (IgA)
		Ab type Leucine zipper motif **References** Clerici2002a • Six sera from HIV-exposed uninfected individuals(EU), HIV-infected individuals and healthy controls were analyzed for IgA Abs – neutralizing activity was observed with total IgA from both EU and HIV+ – the EU IgA exclusively bound to a distinctive epitope within gp41, QARILAV, in the coiled coil pocket important for gp120-gp41 interactions – sera of QAFILAV-immunized BALB/c mice was neutralizing with the dose-dependent behavior similar to 2F5 [Clerici2002a]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
594		gp160 (577–583)	gp41 (582–589)	QARILAV	yes	Vaccine	murine (IgA)
		Vaccine *Vector/Type:* peptide *HIV component:* gp41 *Adjuvant:* keyhole limpit haemocyanin (KLH) **Ab type** Leucine zipper motif **References** Clerici2002a • Six sera from HIV-exposed uninfected individuals(EU), HIV-infected individuals and healthy controls were analyzed for IgA Abs – neutralizing activity was observed with total IgA from both EU and HIV+ – the EU IgA exclusively bound to a distinctive epitope within gp41, QARILAV – sera of QAFILAV-immunized BALB/c mice was neutralizing with the dose-dependent behavior similar to 2F5 [Clerici2002a]					
595	1F11	gp160 (578–612)	gp41 (579–613 BH10)	ARILAVERYLKDQQLLGIWGCSGKL-ICTTAVPWNA	no	HIV-1 infection	human (IgG1κ)
		Donor H. Katinger, Inst. Appl. Microbiol., Vienna, Austria **References** Buchacher1992, Buchacher1994 • 1F11: Generated by electrofusion of PBL from HIV-1 positive volunteers with CB-F7 cells [Buchacher1994]					
596	1H5	gp160 (578–612)	gp41 (579–613 BH10)	ARILAVERYLKDQQLLGIWGCSGKL-ICTTAVPWNA	no	HIV-1 infection	human (IgG1κ)
		References Buchacher1992, Buchacher1994 • 1H5: Generated by electrofusion of PBL from HIV-1 positive volunteers with CB-F7 cells [Buchacher1994]					
597	3D9	gp160 (578–612)	gp41 (579–613 BH10)	ARILAVERYLKDQQLLGIWGCSGKL-ICTTAVPWNA	no	HIV-1 infection	human (IgG1κ)
		Donor H. Katinger, Inst. Appl. Microbiol., Vienna, Austria **References** Buchacher1992, Buchacher1994 • 3D9: Generated by electrofusion of PBL from HIV-1 positive volunteers with CB-F7 cells [Buchacher1994]					
598	4B3	gp160 (578–612)	gp41 (579–613 BH10)	ARILAVERYLKDQQLLGIWGCSGKL-ICTTAVPWNA	no	HIV-1 infection	human (IgG1λ)
		Donor H. Katinger, Inst. Appl. Microbiol., Vienna, Austria **References** Buchacher1992, Buchacher1994, Chen1994b • 4B3: Generated by electrofusion of PBL from HIV-1 positive volunteers with CB-F7 cells [Buchacher1994]					
599	4D4	gp160 (578–612)	gp41 (579–613 BH10)	ARILAVERYLKDQQLLGIWGCSGKL-ICTTAVPWNA	no	HIV-1 infection	human (IgG1λ)
		Donor H. Katinger, Inst. Appl. Microbiol., Vienna, Austria and Viral Testing Systems, Houston, TX **References** Buchacher1992, Buchacher1994, Chen1994b, Sattentau1995c, Binley1999 • 4D4: Generated by electrofusion of PBL from HIV-1 positive volunteers with CB-F7 cells [Buchacher1994] • 4D4: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes [Binley1999]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
600	4G2	gp160 (578–612)	gp41 (579–613 BH10)	ARILAVERYLKDQQLLGIWGCSGKL-ICTTAVPWNA	no	HIV-1 infection	human (IgG1κ)
		Donor H. Katinger, Inst. Appl. Microbiol., Vienna, Austria **References** Buchacher1992, Buchacher1994 • 4G2: Generated by electrofusion of PBL from HIV-1 positive volunteers with CB-F7 cells [Buchacher1994]					
601	polyclonal	gp160 (579–589)	gp41 (586–596 IIIB)	RILAVERYLKD		Vaccine	murine, rabbit
		Vaccine *Vector/Type:* peptide *HIV component:* gp41 *Adjuvant:* BSA **Ab type** C-domain **References** Xiao2000b • Strong epitope-specific neutralizing antibody responses were induced using the peptide C(RILAVERYLKD)_2-BSA, but not full gp160 [Xiao2000b]					
602	polyclonal	gp160 (579–589)	gp41 (586–596)	RILAVERYLKD		Vaccine	rabbit (Ig)
		Vaccine *Vector/Type:* polyepitope, protein *HIV component:* gp160 *Adjuvant:* BSA **Ab type** N-term **References** Lu2000c, Lu2000b • High titer response to ELDKWA and RILAVERYLKD was observed upon vaccination with multiple-epitope vaccine CG-GPGRAFY-G-ELDKWA-G-RILAVERYLKD conjugated to BSA, a weak response to GPGRAFY – immunization with CG-(ELDKWA-GPGRAFY)_2-K was also tried, yielding a strong Ab response to both ELDKWA and GPGRAFY – gp160 vaccination yielded strong Ab response but not to any of the peptides studied here [Lu2000c, Lu2000b]					
603	polyclonal	gp160 (579–599)	gp41 (583–604)	RILAVERYLKDQQLLGIWGCS	no	Vaccine	rabbit
		Vaccine *Vector/Type:* protein *HIV component:* desialylated gp160 **References** Benjouad1993 • MAbs raised against desialylated HIV-1 gp160 cross-react with HIV-2 gp140 due to immunodominant conserved epitope in gp41 [Benjouad1993]					
604	2A2/26	gp160 (579–601)	gp41 (584–606 BRU)	RILAVERYLKDQQLLGIWGCSGK		Vaccine	murine (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* gp41 **References** Poumbourios1992, Poumbourios1995 • 2A2/26: Immunodominant region, binds both oligomer and monomer [Poumbourios1992] • 2A2/26: Delta 550-561 (Delta LLRAIEAQQHLL), a region important for oligomer formation diminishes binding, Delta (550-561 +571-581) abrogates binding [Poumbourios1995]					
605	50-69 (SZ-50.69)	gp160 (579–603)	gp41 (579–603 BH10)	RILAVERYLKDQQLLGIWGCSGKLI	no	HIV-1 infection	human (IgG2κ)
		Ab type cluster I **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU, NY **References** Till1989, Pinter1989, Gorny1989, Xu1991, Robinson1991, Sattentau1991, Eddleston1993, Spear1993, Laal1994, Chen1995, Sattentau1995c, Manca1995a, McDougal1996, Poignard1996a, Binley1996, Klasse1996, Stamatatos1997, Boots1997, Hioe1997b, Mitchell1998, Gorny2000b, Gorny2000a, Nyambi2000, Zwick2001b, Verrier2001 • 50-69: Combined with deglycosylated A chain of ricin is toxic to lines of HIV-infected T cells (H9) and monocytes (U937) [Till1989] • 50-69: Reacts preferentially with gp160 oligomer, compared to gp41 monomer [Pinter1989] • 50-69: Kills HIV-infected cells when coupled to deglycosylated ricin A chain [Gorny1989] • 50-69: The epitope is affected by the conformation conferred by the two cysteines at amino acids 598 and 604 [Xu1991] • 50-69: Enhances HIV-1 infection in vitro – synergizes with huMAb 120-16 in vitro to enhance HIV-1 infection to level approaching that found in polyclonal anti-HIV serum [Robinson1991]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 50-69: Two fold increase in binding to gp120 in the presence of bound sCD4 [Sattentau1991]
- 50-69: Called SZ-50.69 – binds to an epitope within aa 579-613 [Eddleston1993]
- 50-69: Did not mediate deposition of complement component C3 on HIV infected cells unless cells were pre-incubated with sCD4 – complement mediated virolysis of MN and IIIB in the presence of sCD4 [Spear1993]
- 50-69: Epitope described as cluster I, 601-604, conformational – does not neutralize IIIB or synergize neutralization by anti-V3 MAb 447-52D or by CD4 BS MAbs [Laal1994]
- 50-69: One of several anti-gp41 MAbs that bind to a gp41-maltose binding fusion protein designed to study the leucine zipper domain of gp41, showing that the construct has retained aspects of normal gp41 conformation [Chen1995]
- 50-69: Preferentially binds oligomer – binding increased after pretreatment of infected cells with sCD4 – binding domain overlaps site that is critical for gp120-gp41 association [Sattentau1995c]
- 50-69: Virions complexed to gp41 Ab facilitate presentation of p66 RT epitopes to Th cells [Manca1995a]
- 50-69: Does not neutralize HIV-1 LAI [McDougal1996]
- 50-69: Prebinding of anti-V3, and CD4i MAbs 48d and 17b, but not anti-V2 neutralizing MAbs, expose the 50-69 epitope [Poignard1996a]
- 50-69: Binds to a linear epitope located in the cluster I region – binding of 50-69 and 240-D inhibited by Fabs A1, A4, M8B, M26B, M12B and T2 [Binley1996]
- 50-69: Used to test exposure of gp41 upon sCD4 binding [Klasse1996]
- 50-69: Binding of anti-gp120 MAbs IgG1b12 or 654-30D does not mediate significant exposure of the gp41 epitopes for MAbs 2F5 and 50-69 [Stamatatos1997]
- 50-69: Abs that recognize discontinuous epitopes can identify mimotopes from a phage peptide display library – 50-69 maps to an immunodominant domain in gp41 – three groups of peptides were selected, one which seems most closely related to gp41 sequence peptide consensus is WGCxx(RK)(x n)LxC – the analogous gp41 sequence WGCSGKLIC is present in most M group clades, except D with a common L to H substitution [Boots1997]
- 50-69: Mutations in BH10 gp160, W596Y and T605A, as well as deletions of 605-609 (TTAVP) and 597-609 (GCSGKLICTTAVP), abrogate binding of enhancing MAbs 86, 240D, 50-69, and 246-D – 5/6 enhancing MAbs identified to date bind to the immunodominant region 579-613 – identifies non-contiguous W596-G597-C598 and C604-T605 as minimal epitope [Mitchell1998]
- 50-69: A cluster I epitope that binds to rgp41 567-647, recognizes a peptide N51-C43 complex trimer of heterodimers that approximates the core of the fusogenic form of gp41 – this MAb doesn't react with either of the peptides N51 or C43 individually – MAbs 50-69 and 1367 had similar properties – MAb 50-69 bound the fusogenic form of the protein in liquid phase [Gorny2000b]
- 50-69: Binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, but gp41 MAb 50-69 bound with a 5 fold preference for the oligomer, while other gp41 MAbs (1367, 98-6, 167-D, 1281, 1342, and 1379) did not show a preference [Gorny2000a]
- 50-69: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 5 cluster I anti-gp41 MAbs which showed good cross clade reactivity – 50-69 bound the majority of isolates although binding was moderate to weak – specifies discontinuous binding site range as aa 579-613 [Nyambi2000]
- 50-69: This paper primarily concerns 4E10 and Z13, MAbs that both bind proximally to the 2F5 binding site to a conserved epitope, and that neutralize some primary isolates from clades B, C, and E – MAb 50-69 binding to infected cells is enhanced by sCD4, while 4E10 and Z13 binding is essentially unaltered [Zwick2001b]
- 50-69: A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6 – six gave significant neutralization at 2 to 10 ug/ml: 2F5, 50-69, IgG1b12, 447-52D, 2G12, and 670-D six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98-6, and 1281 – no synergy, only additive effects were seen for pairwise combinations of MAbs, and antagonism was noted between gp41 MAbs 50-69 and 98-6, as well as 98-6 and 2F5 [Verrier2001]
- 50-69: NIH AIDS Research and Reference Reagent Program: 531

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
606	9-11	gp160 (579–604)	gp41 (584–609)	RILAVERYLKDQQLLGIWGCSGKLIC		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* gp160 **References** Mani1994 • 9-11: required the C-C disulfide bridge and loop formation, can bind simultaneously with 41-1 [Mani1994]					
607	98-43	gp160 (579–604)	gp41 (579–604 HXB2)	RILAVERYLKDQQLLGIWGCSGKLIC	no	HIV-1 infection	human (IgG2κ)
		References Pinter1989, Gorny1989, Tyler1990, Xu1991 • 98-43: Reacts equally well with oligomer and monomer [Pinter1989] • 98-43: Poor ADCC (in contrast to MAb 120-16, gp41(644-663)) [Tyler1990] • 98-43: 579-604 binds in the immunodominant region [Xu1991] • 98-43: NIH AIDS Research and Reference Reagent Program: 1241					
608	41-1 (41.1)	gp160 (579–608)	gp41 (584–609)	RILAVERYLKDQQLLGIWGCSGKLI-CTTAV		Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* protein *HIV component:* gp160 **References** Gosting1987, Dalgleish1988, Pincus1991, Pincus1993a, Mani1994, Pincus1996, Pincus1998 • 41-1: This antibody to gp41(584-609) [Mani1994] seems to have been named the same as a different MAb to gp41(735-752 IIIB) [Dalgleish1988] • 41-1: Also called 41.1, although possibly not, the literature is confusing because two gp41 MAbs that bind to this region with similar names (dash versus period) are listed as murine and human • 41-1: Broadly reactive [Gosting1987] • 41-1: This antibody seems to have been named the same as a different MAb to gp41(735-752) [Dalgleish1988] • 41-1: Efficacious as an immunotoxin when coupled to RAC – gave linear epitope as gp160 579-603 [Pincus1991] • 41-1: Called 41.1, and described as a human MAb – cross-competes with 41.4 – sCD4 enhances the efficacy of immunotoxins in vitro 30-fold – MAb was coupled to ricin A chain (RAC) [Pincus1993a] • 41-1: Did not require the C-C disulfide bridge and loop formation, can bind simultaneously with 9-11 [Mani1994] • 41-1: Called 41.1, and described as a human MAb, binding 579-604 – a panel of immunotoxins was generated by linking Env MAbs to ricin A – immunotoxins mediated cell killing, but killing was not directly proportional to binding [Pincus1996]					
609	41.4	gp160 (579–608)	gp41 (584–609)	RILAVERYLKDQQLLGIWGCSGKLI-CTTAV			
		Donor Jan McClure, Bristol-Myers Squibb Pharmaceutical Res Inst, Seattle, WA **References** Pincus1993a • 41.4: Binds to peptide weakly, but to gp160 with higher affinity than 41.1, and cross-competes with 41.1 – probably conformational – MAb was coupled to ricin A chain (RAC) – sCD4 enhances the efficacy of immunotoxins in vitro 30-fold [Pincus1993a]					
610	Fab A1	gp160 (579–608)	gp41 (584–609 LAI)	RILAVERYLKDQQLLGIWGCSGKLI-CTTAV	no	HIV-1 infection	human (IgG1κ)
		References Binley1996 • Fab A1: Binds to cluster I region – competes with MAbs 240-D and 50-69 – conformation sensitive – variable regions sequenced [Binley1996]					
611	Fab A4	gp160 (579–608)	gp41 (584–609 LAI)	RILAVERYLKDQQLLGIWGCSGKLI-CTTAV	no	HIV-1 infection	human (IgG1κ)
		References Binley1996					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• Fab A4: Binds to cluster I region – competes with MAbs 240-D and 50-69 – conformation sensitive – variable regions sequenced [Binley1996]					
612	Fab M12B	gp160 (579–608)	gp41 (584–609 LAI)	RILAVERYLKDQQLLGIWGCSGKLI-CTTAV	no	HIV-1 infection	human (IgG1κ)
		References Binley1996 • Fab M12B: Binds to cluster I region – competes with MAbs 240-D and 50-69 – conformation sensitive – variable regions sequenced [Binley1996]					
613	Fab M26B	gp160 (579–608)	gp41 (584–609 LAI)	RILAVERYLKDQQLLGIWGCSGKLI-CTTAV	no	HIV-1 infection	human (IgG1κ)
		References Binley1996 • Fab M26B: Binds to cluster I region – competes with MAbs 240-D and 50-69 – conformation sensitive – variable regions sequenced [Binley1996]					
614	Fab M8B	gp160 (579–608)	gp41 (584–609 LAI)	RILAVERYLKDQQLLGIWGCSGKLI-CTTAV	no	HIV-1 infection	human (IgG1κ)
		References Binley1996 • Fab M8B: Binds to cluster I region – competes with MAbs 240-D and 50-69 – conformation sensitive – variable regions sequenced [Binley1996]					
615	Fab T2	gp160 (579–608)	gp41 (584–609 LAI)	RILAVERYLKDQQLLGIWGCSGKLI-CTTAV	no	HIV-1 infection	human (IgG1κ)
		References Binley1996 • Fab T2: Binds to cluster I region – competes with MAbs 240-D and 50-69 – conformation sensitive – variable regions sequenced [Binley1996]					
616	86 (No. 86)	gp160 (579–613)	gp41 (586–620 IIIB)	RILAVERYLKDQQLLGIWGCSGKLI-CTTAVPWNAS	no	HIV-1 infection	human (IgG1κ)
		Donor Evan Hersh and Yoh-Ichi Matsumoto **References** Sugano1988, Robinson1990b, Robinson1990c, Pincus1991, Moran1993, Wisnewski1996, Mitchell1998 • 86: Reacts with gp41 and also reacted weakly with gp120 [Sugano1988] • 86: Antibody dependent enhancement (ADE) of HIV-1 IIIB infectivity in the presence of complement [Robinson1990b] • 86: Peptide 586-620 blocks complement mediated ADE [Robinson1990c] • 86: Poor immunotoxin activity when coupled to RAC – peptide binding stated to be aa 579-603 [Pincus1991] • 86: Heavy (V HI) and light (V kappaI) chain sequenced – enhancing activity – similar germline sequence to MAb S1-1, but very different activity [Moran1993] • 86: 86 is V H1 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals [Wisnewski1996] • 86: Mutations in BH10 gp160, W596Y and T605A, as well as deletions of 605-609 (TTAVP) and 597-609 (GCSGKLICTTAVP), abrogate binding of enhancing MAbs 86, 240D, 50-69, and 246-D – 5/6 enhancing MAbs identified to date bind to the immunodominant region 579-613 [Mitchell1998] • 86: NIH AIDS Research and Reference Reagent Program: 380					
617	polyclonal	gp160 (580–597)	gp41 (584–602)	ILAVERYLKDQQLLGIWG	no	HIV-1 infection	human
		References Petrov1990 • Immunodominant and broadly reactive peptide [Petrov1990]					
618	V10-9	gp160 (580–613)	gp41 (586–620 IIIB)	ILAVERYLKDQQLLGIWGCSGKLIC-TTAVPWNAS	no	HIV-1 infection	human (IgG1κ)
		References Robinson1990b, Robinson1990c					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• V10-9: Antibody dependent enhancement (ADE) of HIV-1 IIIB infectivity, synergistically enhanced by MAb 120-16 [Robinson1990b] • V10-9: Peptide 586-620 blocks complement mediated ADE [Robinson1990c]					
619	polyclonal	gp160 (582–589)	gp41 (589–596)	AVERYLKD		HIV-1 infection	human
		References Klasse1991 • Substitutions and deletions in peptide 583-599 were systematically studied – alterations in AVERYLKD abrogated the antigenicity of peptides with most of 14 human sera [Klasse1991]					
620	polyclonal	gp160 (584–604)	gp41 (74–94)	ERYLKDQLLGIWGCSGKLIC		HIV-1 infection	human
		References Shafferman1989 • Immunogenic domain useful for diagnostics [Shafferman1989]					
621	polyclonal	gp160 (584–612)	gp41 (587–617 BRU)	ERYLKDQQLLGIWGCSGKLICTTAV-PWNA	no	HIV-1 infection	human
		References Hernandez2000 • Chimeric peptide combining two peptides gp160(495-516 and 584-612) served as a specific and broadly reactive antigen for diagnostic detection of HIV-1 [Hernandez2000]					
622	2F11	gp160 (589–600)	gp41 (589–600 HXB2)	DQQLLGIWGCSG	no	HIV-1 infection	human (IgG1)
		References Eaton1994, Enshell-Seijffers2001 • 2F11: Enhances infectivity even in the absence of complement – does not mediate ADCC or neutralize virus [Eaton1994] • 2F11: Monoclonal antibodies to this epitope have distinct phenotypes—41-7 and 1B8.env were found to be not neutralizing, 2F11 possibly enhancing, and clone 3 beneficial [Enshell-Seijffers2001].					
623	246-D (SZ-246.D, 246, 246D)	gp160 (590–597)	gp41 (579–604 HXB2)	qqLLGIWg	no	HIV-1 infection	human (IgG1κ)
		Ab type cluster I **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU Med Center, NY, NY **References** Xu1991, Robinson1991, Spear1993, Eddleston1993, Forthal1995, Manca1995a, Saarloos1995, Earl1997, Hioe1997b, Gorny2000b, Nyambi2000, Verrier2001, Gorny2002, Edwards2002 • 246-D: Fine mapping indicates core is LLGI [Xu1991] • 246-D: Did not mediate deposition of complement component C3 on HIV infected cells unless cells were pre-incubated with sCD4 [Spear1993] • 246-D: No neutralizing activity, some enhancing activity [Robinson1991] • 246-D: Called SZ-246.D [Eddleston1993] • 246-D: No neutralizing activity, both ADCC and viral enhancing activity [Forthal1995] • 246-D: Virions complexed to gp41 Ab facilitate presentation of p66 RT epitopes to Th cells [Manca1995a] • 246-D: Ab-mediated activation of complement on HIV+ cells is higher than Ab independent activation—what has been termed "Ab independent" in fact results in part from IgM in normal human serum that is HIV-cross-reactive [Saarloos1995] • 246-D: Mutations in BH10 gp160, W596Y and T605A, as well as deletions of 605-609 (TTAVP) and 597-609 (GCSGKLICTTAVP), abrogate binding of enhancing MAbs 86, 240D, 50-69, and 246-D – 5/6 enhancing MAbs identified to date bind to the immunodominant region 579-613 [Mitchell1998] • 246-D: Four primary isolates showed distinct patterns of sensitivity to neutralization by polyclonal sera or plasma and MAbs – BZ167 was the only isolate inhibited by all polyclonal sera and plasma tested, and was also neutralized by 8/17 MAbs, in particular anti-V3 loop (419-D, 447-52D, 782-D, and 838-D), anti-CD4bd (559/64-D, 654-D and 830-D and a cluster II of gp41 directed MAb (98-6) – isolates 92HT593 and 91US056 were neutralized by V3 loop (419-D, and 447-52D)and cluster II gp41 (98-6) MAbs at higher concentrations and 246-D neutralized 91US056 – US4 was neutralized by some of the polyclonal sera/plasma tested and not at all by MAbs individually or by a cocktail of ten MAbs consisting of 419-D, 447-52D, 782-D, 838-D, 559/64-D, 654-D, 450-D, 670-D, 1281-D and 98-6 [Hioe1997b]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 246-D: This antibody, along with murine MAb D61, can be blocked by any of a group of 8 conformational MAbs (M10, D41, D54, T4, T6, T9, T10 and T35) [Earl1997] • 246-D: Core epitope aa 591 to 597, a cluster I epitope that does not bind to either a peptide complex that approximates the core of the fusogenic form of gp41 or the individual peptides N51 and C43 that form this structure – MAbs 181-D and 246-D had similar properties [Gorny2000b] • 246-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 5 cluster I anti-gp41 MAbs which showed good cross clade reactivity – 246-D bound strongly or moderately to all 26 HIV-1 group M clades viruses tested and showed the strongest binding of all anti-Env MAbs tested, including the V3 and C5 region MAbs – notes core epitope as LLGI – no neutralizing activity was observed when 246-D was tested with five isolates [Nyambi2000] • 246-D: A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6 – six gave significant neutralization at 2 to 10 ug/ml: 2F5, 50-69, IgG1b12, 447-52D, 2G12, and 670-D six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98-6, and 1281 – no synergy, only additive effects were seen for pairwise combinations of MAbs, and antagonism was noted between gp41 MAbs 50-69 and 98-6, as well as 98-6 and 2F5 [Verrier2001] • 246-D: Called 246 – Conformation-dependent anti-V3 loop Abs may be more cross-reactive, so six new V3 MAbs were generated – the six new MAbs all bind to the tip of the V3 loop and cross-compete with the MAb 447-52D and are conformationally sensitive – MAbs showed cross-clade binding to native, intact virions and the strength binding was highly correlated with percent neutralization using the ghost cell or PHA blast assay – five well-characterized MAbs were used as controls: anti-V3 447-52D (anti-V3 MAb for competition and neutralization studies), 654 (anti-CD4BS used as a conformation-sensitive MAb control), 1331A (anti-C5 used as a linear binding site MAb control), and MAb 246 (anti-gp41 MAb that bound to primary isolates of all clades tested, A, B, C, D, F and CRF01 (clade E) [Gorny2002] • 246-D: Called 246D – Truncation of the gp41 cytoplasmic domain of X4, R5, and X4R5 viruses forces a conformation that more closely resembles the CD4 bound state of the external Envelope, enhancing binding of CD4i MAbs 17b and 48d and of CD4BS MAbs F105, b12, and in most cases of glycosylation site dependent MAb 2G12 and the anti-gp41 MAb 246D – in contrast, binding of the anti-V2 MAb 697D and the anti-V3 MAb 694/98D were not affected – viruses bearing the truncation were more sensitive to neutralization by MAbs 48d, b12, and 2G12 – the anti-C5 MAb 1331A was used to track levels of cell surface expression of the mutated proteins [Edwards2002] • 246-D: NIH AIDS Research and Reference Reagent Program: 1245			
624	9G5A	gp160 (591–594)	gp41 (596–599 IIIB)	QLLG		anti-idiotype	murine (IgM)
		References Lopalco1993, Beretta1994 • 9G5A: Anti-idiotype to gp120 C terminus (C5 region) MAb M38 [Lopalco1993]					
625	181-D (SZ-181.D)	gp160 (591–597)	gp41 (591–597 HXB2)	qLLGIWg	no	HIV-1 infection	human (IgG2κ)
		Ab type cluster I **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU, NY **References** Xu1991, Robinson1991, Eddleston1993, Forthal1995, Fontenot1995, Gorny2000b, Nyambi2000 • 181-D: Fine mapping indicates core is LLGIW [Xu1991] • 181-D: No enhancing or neutralization activity [Robinson1991] • 181-D: Called SZ-181.D [Eddleston1993] • 181-D: No neutralizing, no ADCC, and no viral enhancing activity [Forthal1995] • 181-D: Core epitope aa 591 to 597, a cluster I epitope that does not bind to either a peptide complex that approximates the core of the fusogenic form of gp41 or the individual peptides N51 and C43 that form this structure – MAbs 181-D and 246-D had similar properties [Gorny2000b] • 181-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 5 cluster I anti-gp41 MAbs which showed good cross clade reactivity – 181-D bound the majority of isolates although binding was moderate to weak [Nyambi2000]					
626	polyclonal	gp160 (591–608)	gp41	QQLLGIWGCSGKLICTTA	no	HIV-1 infection	human (IgG)
		References Parekh2002					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• A simple enzyme immunoassay (EIA) that detects increasing levels of anti-HIV IgG after seroconversion can be used for detecting recent HIV-1 infection – longitudinal specimens from 139 incident infections in the US and Thailand were used in the study – the method was generally applicable for HIV-1 subtypes A, B, C, D and E(CRF01) [Parekh2002]					
627	240-D (F240)	gp160 (592–600)	gp41 (592–600 HXB2)	LLGIWGCSG	no	HIV-1 infection	human
		Ab type cluster I **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU, NY **References** Xu1991, Robinson1991, Spear1993, Binley1996, Wisnewski1995, Wisnewski1996, Mitchell1998, Nyambi2000 • 240-D: Fine mapping indicates core is IWG [Xu1991] • 240-D: No neutralizing activity, some enhancing activity [Robinson1991] • 240-D: Did not mediate deposition of complement component C3 on HIV infected cells [Spear1993] • 240-D: Binds to a linear epitope located in the cluster I region – binding of 50-69 and 240-D inhibited by Fabs A1, A4, M8B, M26B, M12B and T2 [Binley1996] • 240-D: Called F240 – F240 in V H3 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals [Wisnewski1996] • 240-D: Mutations in BH10 gp160, W596Y and T605A, as well as deletions of 605-609 (TTAVP) and 597-609 (GCSGKLICTTAVP), abrogate binding of enhancing MAbs 86, 240D, 50-69, and 246-D – 5/6 enhancing MAbs identified to date bind to the immunodominant region 579-613 [Mitchell1998] • 240-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 5 cluster I anti-gp41 MAbs which showed good cross clade reactivity – 246-D bound strongly or moderately to 24/26 HIV-1 group M clades viruses tested [Nyambi2000] • 240-D: NIH AIDS Research and Reference Reagent Program: 1242				
628	F240	gp160 (592–606)	gp41 (592–606 BH10)	LLGIWGCSGKLICTT	no	HIV-1 infection	human (IgG1κ)
		Ab type cluster I **Donor** L. Cavacina or M. Posner, Dept. of Med. Harvard Med. School, Boston MA, USA **References** Cavacini1998a, York2001 • F240: Seems to be distinct from MAb 240-D, an antibody with a similar epitope in the immunodominant region of gp41 – dose-dependent reactivity with HIV isolates RF, SF2, IIIB, and MN was observed – F240 had no neutralizing activity and enhances infection in the presence of complement – reactivity of F240 is enhanced by preincubation of cells with sCD4 or anti-CD4BS MAb F105 – heavy and light chain variable domains were sequenced, and a strong homology to hu MAb 3D6 was observed, as 3D6 binds to the same epitope, these MAbs may define a human Ab clonotype [Cavacini1998a] • F240: Abs against the V3 loop (50.1, 58.2, 59.1, 257-D, 268-D, 447-52D), CD4BS (IgG1b12, 559-64D, F105), CD4i (17b), and to gp41 (2F5, F240) each showed similar binding efficiency to Env derived from related pairs of primary and TCLA lines (primary: 168P and 320SI, and TCLA: 168C and 320SI-C3.3), but the TCLA lines were much more susceptible to neutralization suggesting that the change in TCLA lines that make them more susceptible to NAbs alters some step after binding [York2001]				
629	D49	gp160 (592–608)	gp41 (597–613)	LLGIWGCSGKLICTTAV		Vaccine	murine
		Vaccine *Vector/Type:* protein *HIV component:* dimeric Env **Ab type** cluster I **References** Earl1994, Earl1997 • D49: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response [Earl1994] • D49: Binding maps to region 597-613: WGCSGKLICTTAVPWNA – immunodominant region containing two Cys residues [Earl1997]					
630	D61	gp160 (592–608)	gp41 (592–608 HXB2)	LLGIWGCSGKLICTTAV		Vaccine	murine
		Vaccine *Vector/Type:* protein *HIV component:* dimeric Env **Ab type** cluster I **Donor** Patricia Earl and Christopher Broder, NIH **References** Earl1994, Richardson1996, Weissenhorn1996, Earl1997, Golding2002b • D61: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response [Earl1994]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• D61: Linear gp41 epitope in the cluster I region – human sera blocked binding in oligomeric ELISA assay to a similar extent for gp41 MAbs D20, D43, D61, and T4 [Richardson1996] • D61: Does not precipitate gp41(21-166), but due to a structural difference in the disulfide bonding region near the two cysteines – the authors propose that this region may change conformation during the activation of the membrane fusion state of the HIV-1 glycoprotein [Weissenhorn1996] • D61: Binding maps to region 597-613: WGCSGKLICTTAVPWNA – immunodominant region containing two Cys residues – this antibody, along with human MAb 246-D, can be blocked by any of a group of 8 conformational MAbs (M10, D41, D54, T4, T6, T9, T10 and T35) – members of this competition group are blocked by sera from HIV-1+ individuals [Earl1997] • D61: The fusion process was slowed by using a suboptimal temperature (31.5 C) to re-evaluate the potential of Abs targeting fusion intermediates to block HIV entry – preincubation of E/T cells at 31.5 C enabled polyclonal anti-N-HR Ab and anti-six-helix bundle Abs to inhibit fusion, indicating six-helix bundles form prior to fusion – the preincubation 31.5 C step did not alter the inhibitory activity of neutralizing Abs anti-gp41 2F5, or anti-gp120 2G12, IG1b12, 48d, and 17b – nor did it alter two gp41 MAbs, T9 and D61, inability to inhibit fusion [Golding2002b]				
631	T32	gp160 (592–608)	gp41 (597–613)	LLGIWGCSGKLICTTAV		Vaccine	murine
		Vaccine *Vector/Type:* tetrameric Env *HIV component:* Env **Ab type** cluster I **Donor** Patricia Earl and Christopher Broder, NIH **References** Earl1994, Earl1997 • T32: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response [Earl1994] • T32: Binding maps to region 597-613: WGCSGKLICTTAVPWNA – immunodominant region containing two Cys residues [Earl1997]				
632	T34	gp160 (592–608)	gp41 (597–613)	LLGIWGCSGKLICTTAV		Vaccine	murine
		Vaccine *Vector/Type:* tetrameric Env *HIV component:* Env **Ab type** cluster I **Donor** Patricia Earl and Christopher Broder, NIH **References** Earl1994, Earl1997 • T34: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response – an oligomer with no gp120/gp41 cleavage site was used as the immunogen [Earl1994] • T34: Binding maps to region 597-613: WGCSGKLICTTAVPWNA – immunodominant region containing two Cys residues [Earl1997]				
633	115.8	gp160 (593–604)	gp41 (598–609)	LGLIWGCSGKLIC		Vaccine	murine (IgM)
		Vaccine *Vector/Type:* peptide *HIV component:* gp41 **References** Oldstone1991 • 115.8: Stimulated by immunization with the peptide: LGLIWGCSGKLIC (aa 598-609) – poor reactivity with CSGKLIC – reacts well with longer HIV-2 peptide NSWGCAFRQVC as well as CAFRQVC – disulfide bond between cysteines required [Oldstone1991]				
634	M-1	gp160 (593–604)	gp41 (598–609)	LGIWGCSGKLIC		Vaccine	murine (IgG1, IgG2b)
		Vaccine *Vector/Type:* peptide *HIV component:* gp41 **References** Yamada1991 • M-1: Unlike M-22, did not react to 43-kd protein found in rat and human astrocytes [Yamada1991]					
635	M-11	gp160 (593–604)	gp41 (598–609)	LGIWGCSGKLIC		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* peptide *HIV component:* gp41 **References** Yamada1991 • M-11: Strongly reacted with a cellular 43-kd protein found in rat and human astrocytes as well as with gp41 [Yamada1991]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
636	M-13	gp160 (593–604)	gp41 (598–609)	LGIWGCSGKLIC		Vaccine	murine (IgG2b)
		Vaccine *Vector/Type:* peptide *HIV component:* gp41 **References** Yamada1991 • M-13: Reacted with a cellular 43-kd protein found in rat and human astrocytes as well as with gp41 [Yamada1991]					
637	M-2	gp160 (593–604)	gp41 (598–609)	LGIWGCSGKLIC		Vaccine	murine (IgG2b)
		Vaccine *Vector/Type:* peptide *HIV component:* gp41 **References** Yamada1991 • M-2: Strongly reacted with a cellular 43-kd protein found in rat and human astrocytes as well as with gp41 [Yamada1991]					
638	M-22	gp160 (593–604)	gp41 (598–609)	LGIWGCSGKLIC		Vaccine	murine (IgG2b)
		Vaccine *Vector/Type:* peptide *HIV component:* gp41 **References** Yamada1991 • M-22: Strongest reaction of 12 anti-HIV-1 gp41 MAbs to a cellular 43-kd protein found in rat and human astrocytes [Yamada1991]					
639	M-24	gp160 (593–604)	gp41 (598–609)	LGIWGCSGKLIC		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* peptide *HIV component:* gp41 **References** Yamada1991 • M-24: Strongly reacted with a cellular 43-kd protein found in rat and human astrocytes as well as with gp41 [Yamada1991]					
640	M-25	gp160 (593–604)	gp41 (598–609)	LGIWGCSGKLIC		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* peptide *HIV component:* gp41 **References** Yamada1991 • M-25: Reacted with a cellular 43-kd protein found in rat and human astrocytes as well as with gp41 [Yamada1991]					
641	M-28	gp160 (593–604)	gp41 (598–609)	LGIWGCSGKLIC		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* peptide *HIV component:* gp41 **References** Yamada1991 • M-28: Strongly reacted with a cellular 43-kd protein found in rat and human astrocytes as well as with gp41 [Yamada1991]					
642	M-29	gp160 (593–604)	gp41 (598–609)	LGIWGCSGKLIC		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* peptide *HIV component:* gp41 **References** Yamada1991 • M-29: Unlike M-22, did not react to 43-kd protein found in rat and human astrocytes [Yamada1991]					
643	M-36	gp160 (593–604)	gp41 (598–609)	LGIWGCSGKLIC		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* peptide *HIV component:* gp41 **References** Yamada1991 • M-36: Unlike M-22, did not react to 43-kd protein found in rat and human astrocytes [Yamada1991]					
644	M-4	gp160 (593–604)	gp41 (598–609)	LGIWGCSGKLIC		Vaccine	murine (IgG2b)
		Vaccine *Vector/Type:* peptide *HIV component:* gp41 **References** Yamada1991 • M-4: Unlike M-22, did not react to 43-kd protein found in rat and human astrocytes [Yamada1991]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
645	M-6	gp160 (593–604)	gp41 (598–609)	LGIWGCSGKLIC		Vaccine	murine (IgG2b)
		Vaccine *Vector/Type:* peptide *HIV component:* gp41 **References** Yamada1991 • M-6: Unlike M-22, did not react to 43-kd protein found in rat and human astrocytes [Yamada1991]					
646	polyclonal α598-609	gp160 (594–601)	gp41 (598–609)	GIWGCSGK		HIV-1 infection	human
		References Poumbourios1992 • alpha(598-609): Affinity purified from HIV-1+ plasma – immunodominant region, binds oligomer and monomer [Poumbourios1992]					
647	1B8.env	gp160 (594–604)	gp41 (594–605 HXB2)	GIWGCSGKLIC	no	HIV-1 infection	human (IgG2λ)
		References Banapour1987, Enshell-Seijffers2001 • 1B8.env: Highly conserved epitope recognized by the majority of HIV-1 infected people – MAb does not neutralize [Banapour1987] • 1B8.env: Monoclonal antibodies to this epitope have distinct phenotypes—41-7 and 1B8.env were found to be not neutralizing, 2F11 possibly enhancing, and clone 3 beneficial [Enshell-Seijffers2001].					
648	polyclonal	gp160 (594–609)	gp41 (601–616)	GIWGCSGKLICTTAVP	no	HIV-1 infection	human
		References Petrov1990 • Immunodominant and broadly reactive peptide [Petrov1990]					
649	clone 3	gp160 (597–606)	gp41 (597–606)	GCSGKLICTT	L	HIV-1 infection	human (IgG1)
		References Broliden1989, Cotropia1992, Cotropia1996, Enshell-Seijffers2001 • clone 3: Core binding domain gcsgkLIC – lack of serological activity to this region correlates with rapid progression in infants ([Broliden1989]) [Cotropia1992] • clone 3: Inhibits replication of three diverse HIV-1 laboratory strains, as well as an AZT-resistant isolate [Cotropia1996] • clone 3: Monoclonal antibodies to this epitope have distinct phenotypes—41-7 and 1B8.env were found to be not neutralizing, 2F11 possibly enhancing, and clone 3 beneficial [Enshell-Seijffers2001].					
650	4	gp160 (598–604)	gp41 (598–609)	CSGKLIC		Vaccine	murine (IgG2b)
		Vaccine *Vector/Type:* peptide *HIV component:* gp41 **References** Oldstone1991, Bizub-Bender1994 • There is another MAb with this ID that reacts with integrase [Oldstone1991, Bizub-Bender1994] • 4: Stimulated by immunization with the peptide: LGLIWGCSGKLIC (aa 598-609) – poor cross-reactivity with HIV-2 peptide CAFRQVC – slightly more reactive with longer HIV-2 peptide NSWGCAFRQVC [Oldstone1991]					
651	41-6	gp160 (598–604)	gp41 (598–609)	CSGKLIC		Vaccine	murine (IgG2b)
		Vaccine *Vector/Type:* peptide *HIV component:* gp41 **References** Oldstone1991 • 41-6: Stimulated by immunization with the peptide: LGLIWGCSGKLIC (aa 598-609) – poor cross-reactivity with HIV-2 peptide CAFRQVC – slightly more reactive with LGLIWGCSGKLIC and HIV-2 form NSWGCAFRQVC – disulfide bond between cysteines required [Oldstone1991]					
652	41-7	gp160 (598–604)	gp41 (605–611)	CSGKLIC	no	HIV-1 infection	human (IgG1κ)
		References Bugge1990, Enshell-Seijffers2001 • 41-7: Sera from 6/6 HIV-1 positive, but no HIV-2 positive individuals, interfered with 41-7 binding – Ab does not neutralize [Bugge1990]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 41-7: Monoclonal antibodies to this epitope have distinct phenotypes—41-7 and 1B8.env were found to be not neutralizing, 2F11 possibly enhancing, and clone 3 beneficial [Enshell-Seijffers2001].					
653	68.1	gp160 (598–604)	gp41 (598–609)	CSGKLIC		Vaccine	murine (IgM)
		Vaccine *Vector/Type:* peptide *HIV component:* gp41 **References** Oldstone1991 • 68.1: Stimulated by immunization with the peptide: LGLIWGCSGKLIC (aa 598-609) – cross-reactive with HIV-2 peptide CAFRQVC – more reactive with longer HIV-1 peptide LGLIWGCSGKLIC and HIV-2 peptide NSWGCAFRQVC [Oldstone1991]					
654	68.11	gp160 (598–604)	gp41 (598–609)	CSGKLIC		Vaccine	murine (IgM)
		Vaccine *Vector/Type:* peptide *HIV component:* gp41 **References** Oldstone1991 • 68.11: Stimulated by immunization with the peptide: LGLIWGCSGKLIC (aa 598-609) – cross-reactive with HIV-2 peptide CAFRQVC – more reactive with longer HIV-1 peptide LGLIWGCSGKLIC and HIV-2 peptide NSWGCAFRQVC [Oldstone1991]					
655	75	gp160 (598–604)	gp41 (598–609)	CSGKLIC		Vaccine	rat (IgG)
		Vaccine *Vector/Type:* peptide *HIV component:* gp41 **References** Oldstone1991 • 75: Stimulated by immunization with the peptide: LGLIWGCSGKLIC (aa 598-609) – poor cross-reactivity with HIV-2 peptide CAFRQVC – more reactive with longer HIV-2 peptide NSWGCAFRQVC [Oldstone1991]					
656	polyclonal	gp160 (598–604)	gp41 (603–609)	CSGKLIC		HIV-1 infection	human
		References Enshell-Seijffers2001 • Monoclonal antibodies to this epitope have distinct phenotypes – 41-7 and 1B8.env were found to be not neutralizing, 2F11 possibly enhancing, and clone 3 beneficial – isolated mimotope-presenting phages corresponding to the immunodominant gp41 epitope CSGKLIC were used to study the diversity of polyclonal responses in 30 HIV+ sera, and all but one of the patients reacted showing distinctive variable polyclonal recognition patterns [Enshell-Seijffers2001]					
657	105-732	gp160 (599–606)	gp41 (601–608 HAM112, O group)	KGRLICYT		Vaccine	murine (IgG2b κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* HAM112 (group O) *HIV component:* gp160 **References** Scheffel1999 • 105-732: Overlapping peptides based on group O HAM112 Env were tested for MAb reactivity – MAb 105-732 bound to two overlapping peptides [Scheffel1999]					
658	3D6 (IAM 41-3D6)	gp160 (599–613)	gp41 (604–617 BH10)	SGKLICTTAVPWNAS	no	HIV-1 infection	human (IgG1κ)
		Ab type immunodominant region **Donor** H. Katinger, Inst. Appl. Microbiol., Vienna, Austria and Viral Testing Systems, Houston, TX **References** Felgenhauer1990, He1992, Chen1994b, Sattentau1995c, Stigler1995, Wisnewski1996, Kunert1998, Cavacini1998b, Cavacini1998a, Cavacini1999 • 3D6: Sequence of cDNA encoding V- regions [Felgenhauer1990] • 3D6: Fab fragment crystal structure [He1992] • 3D6: This MAb binds to HIV gp41, and to a 43 kd protein found in human T, B and monocyte cell lines, proposed molecular mimicry [Chen1994b] • 3D6: Called IAM 41-3D6: binding increased after pretreatment of infected cells with sCD4 – binding domain overlaps site that is critical for gp120-gp41 association [Sattentau1995c] • 3D6: Optimum peptide for binding 3D6 Fab was CSGKLICTTAVPW [Stigler1995]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 3D6: 3D6 is V H3 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals [Wisnewski1996] • 3D6: The complete V, J and D(H) domain was sequenced – in contrast the sequences of five neutralizing MAbs, 3D6 had very little somatic mutation, with homologies of 97-98% relative to germline genes [Kunert1998] • 3D6: Binds to the immunodominant region of gp41 – a strong homology between heavy variable domains of hu MAb 3D6 and MAb F20 was observed, these MAbs may define a human Ab clonotype [Cavacini1998a] • 3D6: Cavacini et al. note that both MAbs F223 and 3D6 are anti-HIV-1 Env MAbs that have an autoimmune response and that both use uses VH3 germline genes [Cavacini1999]					
659	F172-D8 (F172-D8, scFvD8)	gp160 (604–615)	gp41 (609–620)	CTTAVPWNASWS?			human
		References Legastelois2000 • F172-D8: As an approach to intercellular immunization using a single-chain variable fragment, scFvD8 was constructed based on the MAb F172-D8, directed at a loop in gp41 between the two heptad repeat regions – intracellular scFvD8 expression decreased gp160 expression and a scFvD8 transfected cell line did not support infection by HIV-1 Ba-L or primary isolates [Legastelois2000]					
660	D50	gp160 (632–655)	gp41 (642–665)			Vaccine	murine
		Vaccine *Vector/Type:* protein *HIV component:* dimeric Env **Ab type** cluster II **Donor** Patricia Earl and Christopher Broder, NIH **References** Earl1994, Binley1996, Richardson1996, Earl1997, Yang2000, Srivastava2002 • D50: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response [Earl1994] • D50: Thought to be a discontinuous epitope recognizing residues between 649-668 – designated cluster II – Fabs D5, D11, G1, T3, M12, M15, S6, S8, S9, S10 block binding [Binley1996] • D50: Richardson suggests this is a linear gp41 epitope [Richardson1996] • D50: Found to bind to a linear peptide, between Env amino acids 642-655 – can be blocked by the conformation dependent MAbs D16, D17, D31, D36, D37, D40, D44, D55, D59, T37, and T45 – the region is in the immunogenic cluster two region – reactive with 9/10 HIV-1 strains tested, all except HIV-1 ADA, in which the change E659D and E662A may result in the loss of binding (ELLE to DLLA) [Earl1997] • D50: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) – gp41 MAbs T4, D12, T3, and D50 bound less efficiently to gp140-GNC4 than did pooled sera, but T4 and D12 recognized the gp140-GNC4 timer equivalently to gp140(-), and T3 and D50 recognized the trimer at greater levels than gp140(-) [Yang2000] • D50: Oligomeric gp140 (o-gp140) derived from R5 primary isolate US4 was characterized for use as a vaccine reagent – D50 was used to capture the o-gp140 for ELISA to test the antigencity of o-gp140 using a panel of well characterized MAbs [Srivastava2002]					
661	5-21-3	gp160 (642–665)	gp41 (642–665 HXB2)	IHSLIEESQNQQEKNEQELLELDK		Vaccine	murine
		Vaccine *Vector/Type:* recombinant protein *HIV component:* gp41 **References** Hunt1990, Scheffel1999 • 5-21-3: Recognizes a contiguous, conformation-dependent epitope in a hydrophilic region [Hunt1990] • 5-21-3: Binds group M gp41, used as a control in a study of group O MAbs [Scheffel1999]					
662	120-16 (SZ-120.16)	gp160 (644–663)	gp41 (644–663 HXB2)	SLIEESQNQQEKNEQELLEL	no	HIV-1 infection	human (IgG2κ)
		References Andris1992, Robinson1990b, Tyler1990, Xu1991, Robinson1991, Eddleston1993, Forthal1995, Wisnewski1996 • 120-16: Antibody dependent enhancement (ADE) of HIV-1 IIIB infectivity, synergistically enhanced by MAb V10-9 [Robinson1990b] • 120-16: Potent ADCC (in contrast to MAb 98-43, gp41(579-604)) [Tyler1990] • 120-16: Less reactive region than AVERY region – most Abs involving this region bound conformational epitopes, this was the only linear one [Xu1991] • 120-16: Synergizes with huMAb 50-69 in vitro to enhance HIV-1 infection [Robinson1991]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 120-16: Called SZ-120.16 [Eddleston1993]
- 120-16: No neutralizing activity, both ADCC and viral enhancing activity [Forthal1995]
- 120-16: 120-16 is V H4 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals [Wisnewski1996]

663 98-6 (SZ-98.6, 98.6) gp160 (644–663) gp41 (644–663 HXB2) SLIEESQNQQEKNEQELLEL no HIV-1 infection human (IgG2κ)

Ab type alpha-helical C-HR, hairpin intermediate **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU, NY

References Pinter1989, Gorny1989, Till1989, Robinson1990b, Tyler1990, Andris1992, Sattentau1991, Robinson1991, Xu1991, Eddleston1993, Spear1993, Tani1994, Laal1994, Chen1995, Forthal1995, Manca1995a, Sattentau1995c, Wisnewski1996, Hioe1997b, Nyambi1998, Gorny2000b, Gorny2000a, Nyambi2000, Taniguchi2000, Verrier2001, Golding2002b

- 98-6: Reacts preferentially with gp160 oligomer, compared to gp41 monomer [Pinter1989]
- 98-6: Kills HIV-infected cells when coupled to deglycosylated ricin A chain [Gorny1989]
- 98-6: Toxic to HIV-infected T cells (H9) and monocytes (U937) when coupled to deglycosylated A chain of ricin [Till1989]
- 98-6: No neutralizing or enhancing activity for HIV-1 IIIB [Robinson1990b]
- 98-6: Serves as target for antibody-dependent cellular cytotoxicity, ADCC [Tyler1990]
- 98-6: Two fold increase in binding to gp120 in the presence of bound sCD4 [Sattentau1991]
- 98-6: No neutralizing or enhancing activity [Robinson1991]
- 98-6: Appeared to be specific for a conformational or discontinuous epitope [Xu1991]
- 98-6: Called SZ-98.6 – binds to a conformational domain within aa 644-663 of gp41, and reacts with astrocytes, as do 167-7 and ND-15G1 [Eddleston1993]
- 98-6: Did not mediate deposition of complement component C3 on HIV infected cells, binding enhanced by sCD4 [Spear1993]
- 98-6: This MAb was expressed as a surface anti-gp41 monoclonal antibody receptor for gp41 on a CD4-negative B-cell line. Transfected cells could bind HIV Envelope, but could not be infected by HIV-1. When CD4 delivered by retroviral constructs was expressed on these cells, they acquired the ability to replicate HIV-1, and sIg/gp41 specifically enhanced viral replication [Tani1994]
- 98-6: Epitope described as cluster II, 644-663, conformational – does not neutralize IIIB or synergize neutralization by anti-V3 MAb 447-52D or by CD4 BS MAbs [Laal1994]
- 98-6: One of several anti-gp41 MAbs that bind to a gp41-maltose binding fusion protein designed to study the leucine zipper domain of gp41, showing that the construct has retained aspects of normal gp41 conformation [Chen1995]
- 98-6: No neutralizing activity, positive ADCC activity, and no viral enhancing activity [Forthal1995]
- 98-6: Virions complexed to gp41 Ab facilitate presentation of p66 RT epitopes to Th cells [Manca1995a]
- 98-6: Preferentially recognizes oligomeric form of gp41 – enhanced binding to HIV-1 infected cells at 37 degrees relative to 4 degrees – addition of sCD4 enhances binding [Sattentau1995c]
- 98-6: 98-6 is V H4 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals [Wisnewski1996]
- 98-6: Four primary isolates showed distinct patterns of sensitivity to neutralization by polyclonal sera or plasma and MAbs – BZ167 was the only isolate inhibited by all polyclonal sera and plasma tested, and was also neutralized by 8/17 MAbs, in particular anti-V3 loop (419-D, 447-52D, 782-D, and 838-D), anti-CD4bd (559/64-D, 654-D and 830-D and a cluster II of gp41 directed MAb (98-6) – isolates 92HT593 and 91US056 were neutralized by V3 loop (419-D, and 447-52D)and cluster II gp41 (98-6) MAbs at higher concentrations – US4 was neutralized by some of the polyclonal sera/plasma tested and not at all by MAbs individually or by a cocktail of ten MAbs consisting of 419-D, 447-52D, 782-D, 838-D, 559/64-D, 654-D, 450-D, 670-D, 1281-D and 98-6 [Hioe1997b]
- 98-6: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – anti-gp41 Abs 98-6, 1367 and 1342 were not able to bind detectably with any of the viruses from any clade [Nyambi1998]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 98-6: 98-6 and 2F5 both bind to a peptide N51-C43 complex trimer of heterodimers that approximates the core of the fusogenic form of gp41, and to C43 alone but not to N51 alone – 98-6 and 2F5 have comparable affinities for C43, but 98-6 has a higher affinity for the complex and the binding of 98-6 is not inhibited by N51 [Gorny2000b] • 98-6: Binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, but gp41 MAb 50-69 bound with a 5 fold preference for the oligomer, while other gp41 MAbs (1367, 98-6, 167-D, 1281, 1342, and 1379) did not show a preference [Gorny2000a] • 98-6: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 cluster II anti-gp41 MAbs – of these 2F5, 167-D, 126-6, and 1281 bound across clades, but usually weakly, while 98-6 and 1342 had poor cross reactivity – Clade D isolates bound most consistently to cluster II MAbs – no neutralizing activity was observed when tested against 5 isolates, but 98-6 did not bind to these isolates [Nyambi2000] • 98-6: The fusogenic form of gp41 is recognized by 98-6, and the epitope is a conformational epitope formed by the interaction of two regions of gp41 which form an alpha-helical bundle [Taniguchi2000] • 98-6: A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6—six gave significant neutralization at 2 to 10 ug/ml: 2F5, 50-69, IgG1b12, 447-52D, 2G12, and 670-D, while six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98-6, and 1281 – no synergy, only additive effects were seen for pairwise combinations of MAbs, and antagonism was noted between gp41 MAbs 50-69 and 98-6, as well as 98-6 and 2F5 [Verrier2001]. • 98-6: The fusion process was slowed by using a suboptimal temperature (31.5 C) to re-evaluate the potential of Abs targeting fusion intermediates to block HIV entry – preincubation of E/T cells at 31.5 C enabled polyclonal anti-N-HR Ab and anti-six-helix bundle Abs to inhibit fusion, indicating six-helix bundles form prior to fusion – 98-6 binds to a C-HR hairpin epitope and blocks fusion when added to a 2 hour E/T preincubation at 31.5 C, but if added after 1 hour, doesn't inhibit – this is in contrast to six-helix bundle Abs 167-D and 1281 that inhibit more efficiently when added after one hour of incubation [Golding2002b] • 98-6: NIH AIDS Research and Reference Reagent Program: 1240				
664	167-7 (SZ-167.7)	gp160 (644–663)	gp41 (644–663)	SLIEESQNQQEKNEQELLEL		HIV-1 infection	human (IgG2λ)
		Ab type cluster II **References** Xu1991, Eddleston1993 • 167-7: Specific for a conformational epitope [Xu1991] • 167-7: Called SZ-167.7 – binds to a conformational domain within aa 644-663 of gp41, and reacts with astrocytes, as do 98-6 and ND-15G1 [Eddleston1993]					
665	ND-15G1	gp160 (644–663)	gp41 (644–663 HXB2)	SLIEESQNQQEKNEQELLEL		HIV-1 infection	human (IgG1κ)
		Ab type cluster II **References** Eddleston1993 • ND-15G1: Mapped to the conformational epitope within aa 644-663, and reacts with astrocytes, as do 98-6 and 167-7 [Eddleston1993]					
666	167-D	gp160 (644–663)	gp41 (644–663 HXB2)	SLIEESQNQQEKNEQELLEL	no	HIV-1 infection	human (IgG1λ)
		Ab type cluster II, six-helix bundle **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU, NY **References** Spear1993, Forthal1995, Gorny2000b, Gorny2000a, Nyambi2000, Golding2002b • 167-D: Did not mediate deposition of complement component C3 on HIV infected cells – complement mediated virolysis of MN and IIIB in the presence of sCD4 [Spear1993] • 167-D: No neutralizing activity, no ADCC activity, and no viral enhancing activity [Forthal1995] • 167-D: Virions complexed to gp41 Ab facilitate presentation of p66 RT epitopes to Th cells [Manca1995a]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 167-D: This cluster II MAb binds to a conformational epitope in the region 644-663 – like most cluster II MAbs (126-6, 167-D, 1281, 1342, and 1379 all reacted similarly) it binds to a peptide N51-C43 complex trimer of heterodimers that approximates the core of the fusogenic form of gp41, but not to C43 nor to N51 alone [Gorny2000b]
- 167-D: Binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, but gp41 MAb 50-69 bound with a 5 fold preference for the oligomer, while other gp41 MAbs (1367, 98-6, 167-D, 1281, 1342, and 1379) did not show a preference [Gorny2000a]
- 167-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 cluster II anti-gp41 MAbs – of these 2F5, 167-D, 126-6, and 1281 bound across clades, but usually weakly, while 98-6 and 1342 had poor cross reactivity – Clade D isolates bound most consistently to cluster II MAbs [Nyambi2000]
- 167-D: The fusion process was slowed by using a suboptimal temperature (31.5 C) to re-evaluate the potential of Abs targeting fusion intermediates to block HIV entry – preincubation of E/T cells at 31.5 C enabled polyclonal anti-N-HR Ab and anti-six-helix bundle Abs to inhibit fusion, indicating six-helix bundles form prior to fusion – 98-6 binds to a C-HR hairpin epitope and blocks fusion when added to a 2 hour E/T preincubation at 31.5 C, but if added after 1 hour, doesn't inhibit – this is in contrast to six-helix bundle Abs 167-D and 1281 that inhibit more efficiently when added after one hour of incubation [Golding2002b]

667	2F5 (IAM 2F5, IAM-41-2F5, IAM2F5, c2F5)	gp160 (656–671)	gp41 (662–667 BH10)	NEQELLELDKWASLWN	L P	HIV-1 infection	human (IgG3κ)

Ab type adjacent to cluster II **Donor** Hermann Katinger, Institute of Applied Microbiology, Vienna, or Polymun Scientific Inc., Vienna, Austria, or Viral Testing Systems Corp., Houson TX

References Buchacher1992, Muster1993, Allaway1993, Klasse1993a, Purtscher1994, Laal1994, Buchacher1994, D'Souza1994, Conley1994b, Thali1994, Chen1994b, Muster1994, Beretta1994, D'Souza1995, Trkola1995, Sattentau1995c, Moore1995b, Neurath1995, Kessler1995, Calarota1996, McKeating1996a, Poignard1996b, Sattentau1996, Conley1996, Pincus1996, McKeating1996b, Stoiber1996, Purtscher1996, Schutten1997, D'Souza1997, Mo1997, Li1997, Kessler II1997, Moore1997, Mascola1997, Stamatatos1997, Turbica1997, Ugolini1997, Burton1997, Earl1997, Gorny1997, Andrus1998, Mondor1998, Connor1998, Parren1998a, Yang1998, Trkola1998, Fouts1998, Ernst1998, Takefman1998, Li1998, Jiang1998, Parren1998b, Geffin1998, Kunert1998, Frankel1998, Montefiori1999, Poignard1999, Beddows1999, Muhlbacher1999, Parren1999, Mascola1999, Mascola2000, Baba2000, Robert-Guroff2000, Gorny2000b, Kunert2000, Liao2000, Lu2000c, Lu2000b, Nyambi2000, Park2000, Pai2002, Sanhadji2000, Coeffier2000, Xiao2000c, Yang2000, Si2001, Dong2001, Kolchinsky2001, Tumanova2001, York2001, Zwick2001b, Zwick2001c, Mascola2001, Barnett2001, Moore2001, Zeder-Lutz2001, Parker2001, Spenlehauer2001, Verrier2001, Stiegler2001, Hofmann-Lehmann2001, Xu2001, Root2001, Armbruster2002, Srivastava2002, Golding2002b, Schulke2002, Tian2002, Ho2002, Xu2002, Chakrabarti2002, Joyce2002, Clerici2002a, Xiang2002b, Grundner2002, Mascola2002, Kunert2002, Zhang2002, Ferrantelli2002, Liu2002

- 2F5: DKWA defined as the core sequence – highly conserved epitope neutralizing MAb [Buchacher1992, Muster1993]
- 2F5: Synergy with combinations of CD4-based molecules in inhibition of HIV-1 Env mediated cell fusion [Allaway1993]
- 2F5: Called IAM-41-2F5 – reports MAb to be IgG1 – the gp41 mutation 582(Ala to Thr) results in conformational changes in gp120 that confer neutralization resistance to conformationally sensitive neutralizing MAbs – neutralization efficiency of 2F5 is not affected [Klasse1993a]
- 2F5: Broadly reactive neutralizing activity, ELDKWA is relatively conserved – neutralized 2 primary isolates [Purtscher1994]
- 2F5: Failed to show synergy with anti-CD4 binding site IIIB neutralizing antibodies [Laal1994]
- 2F5: MAb generated by electrofusion of PBL from HIV-1 positive volunteers with CB-F7 cells [Buchacher1994]
- 2F5: Included in a multi-lab study for antibody characterization binding and neutralization assay comparison [D'Souza1994]
- 2F5: Called IAM-41-2F5 – neutralized lab and primary isolates – t 1/2 dissociation 122 min for the peptide, and 156 min for gp41 – core D(K/R)W – Ab resistant isolate had the sequence KLDNWA [Conley1994b]
- 2F5: gp41 mutation (582 A/T) that reduces neutralization of anti-CD4 binding site MAbs does not alter 2F5's ability to neutralize [Thali1994]
- 2F5: 2F5 epitope ELDKWA inserted into an immunogenic loop in influenza virus hemagglutinin can elicit IIIB, MN and RF neutralizing sera in immunized mice [Muster1994]

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- 2F5: Found to neutralize MN, JRCSF, and two B subtype primary isolates, but not a D subtype primary isolate, by most labs in a multi-laboratory study involving 11 labs [D'Souza1995]
- 2F5: Cross-clade primary virus neutralizing activity – LDKW defined as the core epitope [Trkola1995]
- 2F5: Called IAM 41-2F5 – exposed in the presence of gp120 on the cell surface, while most of gp41 is masked – binds proximal to transmembrane region [Sattentau1995c]
- 2F5: Review: binds to the only generally accepted strong neutralizing epitope outside of gp120, one of only 3 MAbs with strong broad activity against primary viruses, the others are 2G12 and IgG1b12 – unique member of epitope cluster [Moore1995b] and John Moore, per comm 1996
- 2F5: MAb binding decreases the accessibility or alters the conformation of the gp41 fusion domain and of gp120 domains, including the binding site for the CD4 cell receptor [Neurath1995]
- 2F5: Broad cross-clade neutralization of primary isolates – additive neutralization in combination with anti-CD4BS MAb IgG1b12 (Called BM12) [Kessler1995]
- 2F5: Only 4/20 Argentinian and 3/43 Swedish HIV+ sera reacted with LLELDKWASL – sera reacting with peptides that contained ELDKWA tended to have high neutralization titers – the region carboxyl terminal to EDLKWA was found to be more important for polyclonal sera AB binding, 670-675 WNWFDI – 2F5 bound most strongly to the peptide QELLELDKWA [Calarota1996]
- 2F5: ELDKWAS is in a gp41 binding region for the negative regulator of complement factor H (CFH) – Abs to HIV generally do not cause efficient complement-mediated lysis, but binding of 2F5 can interfere with CHF binding, facilitating HIV destruction by complement [Stoiber1996]
- 2F5: Primary isolates from clade A, B, and E are neutralized by 2F5 – neutralization requires the LDKW motif – neutralization resistant isolates or 2F5 selected variants all had substitutions in the D or K [Purtscher1996]
- 2F5: Neutralizes HXB2, primary isolates, and chimeric virus with gp120 from primary isolates in an HXB2 background [McKeating1996b]
- 2F5: Review: one of three MAbs (IgG1b12, 2G12, and 2F5) generally accepted as having significant potency against primary isolates [Poignard1996b]
- 2F5: Review: only four epitopes have been described which can stimulate a useful neutralizing response to a broad spectrum of primary isolates, represented by the binding sites of MAbs: 447-52-D, 2G12, Fab b12, and 2F5 [Sattentau1996]
- 2F5: 2F5 was infused into two chimpanzees which were then given an intravenous challenge with a primary HIV-1 isolate – both became infected, but with delayed detection and prolonged decrease in viral load relative to controls, indicating that preexisting, neutralizing antibodies (passively administered or actively elicited) affect the course of acute-phase virus replication and can be influential after the Ab can no longer be detected in the peripheral circulation [Conley1996]
- 2F5: A panel of immunotoxins were generated by linking Env MAbs to ricin A – immunotoxins mediated cell killing, but killing was not directly proportional to binding [Pincus1996]
- 2F5: Called IAM 2F5 – antibody mediated enhancement or inhibition seemed to be determined by isolate rather than antibody specificity – in this study, only 2F5 inhibited the entry of all the viruses studied, irrespective of their phenotype, and directly proportional to its affinity to monomeric HIV-1 gp160 [Schutten1997]
- 2F5: Of three neutralizing MAbs (257-D, IgG1b12, and 2F5), 2F5 was the only one to inhibit the entry of all viruses studied, both SI and NSI, with a potency proportional to its affinity for monomeric gp126 [Schutten1997]
- 2F5: In a multilab evaluation of monoclonal antibodies, only IgG1b12, 2G12, and 2F5 could neutralize at least half of the 9 primary test isolates at a concentration of < 25 mug per ml for 90% viral inhibition – the isolates with no 2F5 neutralizing susceptibility had the sequences ALGQWA or ELDTWA instead of EDLKWA – 7/9 primary isolates were neutralized, and ALDKWQ and ALDKWA were susceptible to neutralization [D'Souza1997]
- 2F5: A JRCSF variant that was selected for IgG1b12 resistance remained sensitive to MAbs 2G12 and 2F5, for combination therapy [Mo1997]
- 2F5: One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB Env – strong neutralizer of SHIV-vpu+ – all Ab combinations tested showed synergistic neutralization – 2F5 has synergistic response with MAbs 694/98-D (anti-V3), 2G12, b12, and F105 [Li1997]
- 2F5: IgG1b12 was more potent with greater breadth than MAb 2F5 in an infection reduction assay including 35 primary isolates [Kessler II1997]

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- 2F5: Review: MAbs 2F5, 2G12 and IgG1b12 have potential for use in combination with CD4-IgG2 as an immunotherapeutic or immunoprophylactic – homologous MAbs to these are rare in humans and vaccine strategies should consider including constructs that may enhance exposure of these MAbs' epitopes [Moore1997]
- 2F5: Binding of anti-gp120 MAbs IgG1b12 or 654-30D does not mediate significant exposure of the gp41 epitopes for MAbs 2F5 and 50-69 [Stamatatos1997]
- 2F5: Using concentrations of Abs achievable in vivo, the triple combination of 2F5, 2G12 and HIVIG was found to be synergistic to have the greatest breadth and magnitude of response against 15 clade B primary isolates [Mascola1997]
- 2F5: Used to standardize polyclonal response to CD4 BS [Turbica1997]
- 2F5: The only MAb out of a large panel to show no correlation between Viral binding inhibition and neutralization [Ugolini1997]
- 2F5: This review summarizes results about 2F5: it binds extracellularly, near the transmembrane domain, it is the only gp41 MAb that is neutralizing, it reacts with many non-B clade viruses and has a paradoxically weak binding to virus, given the neutralizing titers [Burton1997]
- 2F5: Post-exposure prophylaxis was effective when MAb 694/98-D was delivered 15 min post-exposure to HIV-1 LAI in hu-PBL-SCID mice, but declined to 50% if delivered 60 min post-exposure, and similar time constraints have been observed for HIVIG, 2F5 and 2G12, in contrast to MAb BAT123 that could protect delivered 4 hours post infection [Andrus1998]
- 2F5: This MAb and the results of [Ugolini1997] are discussed – the authors propose that an Ab bound to gp41 would typically project less from the surface of the virion and so be unable to interfere with attachment [Parren1998a]
- 2F5: Ab from gp120 vaccinated individuals prior to infection, who subsequently became HIV infected, could not achieve 90% neutralization of the primary virus by which the individuals were ultimately infected – these viruses were not particularly refractive to neutralization, as determined by their susceptibility to neutralization by MAbs 2G12, IgG1b12, 2F5 and 447-52D [Connor1998]
- 2F5: A neutralization assay was developed based on hemi-nested PCR amplification of the LTR (HNPCR) – LTR-HNPCR consistently revealed HIV DNA and was shown to be a rapid, specific and reliable neutralization assay based on tests with 6 MAbs and 5 isolates [Yang1998]
- 2F5: A wide range of neutralizing titers was observed that was independent of co-receptor usage – 2F5 was the most potent of the MAbs tested [Trkola1998]
- 2F5: Points out that 2G12 and 2F5, potent neutralizing antibodies, were identified by screening for cell surface (oligomeric Envelope) reactivity [Fouts1998]
- 2F5: The ELDKWA epitope was inserted into the antigenic site B of influenza hemagglutinin and expressed on baculovirus infected insect cells, flanked by 3 additional random amino acids, xELDKWAxx – FACS was used to isolate the clone that displayed the epitope with the most markedly increased binding capacity for 2F5, to identify particularly specific immunogenic constructs – PELDKWAPP was a high affinity form selected by FACS [Ernst1998]
- 2F5: Induces complement-mediated lysis in MN but not primary isolates – primary isolates are refractive to CML [Takefman1998]
- 2F5: Neutralization synergy was observed when the MAbs 694/98-D (V3), 2F5 (gp41), and 2G12 (gp120 discontinuous) were used in combination, and even greater neutralizing potential was seen with the addition of a fourth MAb, F105 (CD4 BS) [Li1998]
- 2F5: Used as a control in the study of anti-gp41 MAb NC-1 – 2F5 does not react with HIV-2 gp41 or gp160 [Jiang1998]
- 2F5: MAbs 2G12, 2F5 and b12 are broadly neutralizing, as are some human polyconal sera, but this paper describes a set of primary isolates that are resistant to all three MAbs and 2 broadly neutralizing sera – results indicate that resistance levels of pediatric isolates might be higher than adult isolates – resistance in general did not seem to be conferred by a loss of binding affinity for gp120 or gp41, rather by a more global perturbation of oligomeric Envelope [Parren1998b]
- 2F5: The natural immune response to the epitope of 2F5, ELDKWA, was studied in perinatally infected children and levels of reactivity to this epitope were correlated with absolute CD4 numbers over time and health status – 3/10 children who had no antibody reactivity to ELDKWA had substitutions in the epitope (ALDKWA, ELDQWA, and KLDKWA) – 2F5 competed with the ELDKWA-reactive sera depending on the serum titer [Geffin1998]

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- 2F5: The complete V, J and D(H) domain was sequenced – unlike non-neutralizing anti-gp41 MAb 3D6, five neutralizing MAbs (2F5, 2G12, 1B1, 1F7, and 3D5) showed extensive somatic mutations giving evidence of persistent antigenic pressure over long periods – in contrast to Geffin98, where multiple pediatric sera were found to compete with 2F5, cross-competition was noted to be very rare in sera from HIV+ adults – Kunert et al. propose that because there is a binding site of human complement factor H which overlaps the 2F5 binding site, it may generally be masked from the immune system – 2F5 also has a remarkably long CDR3 loop of 22 amino acids, and this region could not be readily assigned to any described D(H) fragment, leading to the suggestion of recombination of two fragments from novel regions [Kunert1998]
- 2F5: Infection of dendritic cells cultured from CD14+ blood cells or from cadaveric human skin was blocked by neutralizing MAbs IgG1b12, or 2F5 and 2G12 delivered together, but not by control non-neutralizing anti-gp120 MAb 4.8D, indicating that NAbs could interrupt early mucosal transmission events [Frankel1998]
- 2F5: rgp120 derived from a R5X4 subtype B virus was used to vaccinate healthy volunteers and the resulting sera were compared with sera from HIV-1 positive subjects and neutralizing MAbs [Beddows1999]
- 2F5: A meeting summary presented results regarding neutralization –MAbs 2G12 and 2F5 tested for their ability to neutralize primary isolate infection of genetically engineered cell lines (cMAGI and others, presented by T. Matthews, A. Trkola, J. Bradac) – an advantage of such cells lines over PBMCs is that markers (X-Gal) can be added for staining to simplify the assay – the consensus of the meeting was that these engineered cell lines did not improve the sensitivity of detection of primary isolate neutralization – D. Burton and J. Mascola presented results concerning passive immunization and protection of hu-PBL-SCID mice and macaques, respectively, and both found combinations of MAbs that were able to achieve 99% neutralization in vitro corresponded to efficacy in vivo [Montefiori1999]
- 2F5: Hu-PBL-SCID mice were infected with HIV-1s JRCSF and SF162 to study the effect of NAbs on an established infection – no significant differences in the initial rate of decrease in viral load or the plateau levels of viral RNA between the b12 treated and control mice were seen – in most of the Ab treated mice b12 escape mutants were observed with varying patterns of mutations – a combination of b12, 2G12 and 2F5 protected 1/3 mice, and an isolate from one of the other two was resistant to neutralization by all three MAbs [Poignard1999]
- 2F5: In a study of 116 HIV-1+ individuals, Ab reactivity to a peptide encompassing the ELDKWA peptide decreased in CDC stage C patients compared with stage A patients, and longitudinal studies showed a decline in 6/8 patients, while overall Ab reactivity to rec soluble gp160 stayed constant [Muhlbacher1999]
- 2F5: Review of the neutralizing Ab response to HIV-1 [Parren1999]
- 2F5: Combinations of HIVIG, 2F5, 2G12 were administered in passive-transfer experiments 24 hours prior to challenge with pathogenic SHIV 89.6PD – 3/6 animals given HIVIG/2F5/2G12 were completely protected, the others had reduced viremia and normal CD4 counts – 1/3 monkeys given 2F5/2G12 showed transient infection, the other two had reduced viral load – all monkeys that received HIVIG, 2F5, or 2G12 alone became infected and developed high-level plasma viremia, although animals that got HIVIG or 2G12 had a less profound CD4 T cell decline [Mascola1999]
- 2F5: Because HIV-1 is most often transmitted across mucosal surfaces, the ability of passive transfer of infused HIVIG/2F5/2G12 to protect against mucosal exposure of macaques to pathogenic SHIV 89.6PD was studied – HIVIG/2F5/2G12 protected 4/5 animals against vaginal challenge, 2F5/2G12 combined protected 2/5 animals, and 2G12 alone protected 2/4 animals – in contrast, Mascola and co-workers had previously shown single MAbs could not protect against intervenous challenge – Ab treated animals that got infected through vaginal innoculation had low viral loads and only modest declines in CD4 counts – the infused Abs were detected in the nasal, vaginal, and oral mucosa [Mascola2000]
- 2F5: Paper uses IgG1 form of 2F5 – a triple combination of 2F5, F105 and 2G12 effectively neutralized perinatal infection of macaque infants when challenged with SHIV-vpu+ – the plasma half-life was 4.2 +/- 0.8 days [Baba2000]
- 2F5: A mini-review of observations of passive administration of IgG NAbs conferring protection against intervenous or vaginal SHIV challenge, that considers why IgG MAbs might protect against mucosal challenge [Robert-Guroff2000]
- 2F5: MAbs 98-6 and 2F5 both bind to a peptide N51-C43 complex trimer of heterodimers that approximates the core of the fusogenic form of gp41, and to C43 alone but not to N51 alone – 98-6 and 2F5 have comparable affinities for C43, but 98-6 has a higher affinity for the complex and 2F5 may bind to an epitope of C43 that is directly involved with complex formation –and IgG1 rec form of the Ab was used in this study [Gorny2000b]

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- 2F5: 2F5 is a candidate for immunotherapy, but generally IgG1 has a longer half life in humans than IgG3, so the isotype was switched – rec CHO-derived MAb 2F5 IgG1kappa and hybridoma-derived MAb 2F5 IgG3kappa displayed identical specificity, in vitro function, and epitope (ELDKWA) – it remains to be determined if isotype switching will prolongs beta-clearance [Kunert2000]
- 2F5: Low levels of anti-ELDKWA antibodies are observed in HIV-1+ individuals, so a C-domain P2 peptide linked to a carrier was used to immunize mice and rabbits, and stimulated a high-level anti-ELDKWA response [Liao2000]
- 2F5: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain [Zhang2002]
- 2F5: ELDKWA peptide vaccine study [Lu2000c]
- 2F5: ELDKWA peptide vaccine study [Lu2000b]
- 2F5: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 cluster II anti-gp41 MAbs – of these 2F5, 167-D, 126-6, and 1281 bound across clades, but usually weakly, while 98-6 and 1342 had poor cross reactivity – Clade D isolates bound most consistently to cluster II MAbs [Nyambi2000]
- 2F5: Six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i gp120 specific MAbs are 20-100 fold more efficient at neutralizing the sensitive form – gp41 MAbs bind less, and 2F5 behaves the opposite of gp120 MAbs in that it neutralizes the "sensitive" form less efficiently [Park2000]
- 2F5: ELDKWAS co-crystallized bound to the Fab' 2F5 fragment showed the epitope peptide in a type I beta-turn conformation [Pai2002]
- 2F5: 2F5 or sCD4-IgG chimeric immunoadhesin were transferred into 3T3 cells, incorporated into a collagen structure called the neo-organ, and transplanted into SCIDhu mice that were then challenged with MN or LAI – the continuous production of the therapeutic molecules in this context resulted in dramatic reduction of viral load [Sanhadji2000]
- 2F5: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) – gp41 MAbs T4, D12, T3, and D50 bound less efficiently to gp140-GNC4 than did pooled sera, but T4 and D12 recognized the gp140-GNC4 timer equivalently to gp140(-), and T3 and D50 recognized the trimer at greater levels than gp140(-) – 2F5 did not bind efficiently to these constructs, presumably because of the YU2 strain has a substitution in the 2F5 epitope (ALDKWA instead of ELDKWA) [Yang2000]
- 2F5: SHIV-HXBc2 is a neutralization sensitive non-pathogenic virus, and several in vivo passages through monkey's yielded highly pathogenic SHIV KU-1 – HXBc2 and the KU-1 clone HXBc2P3.2 differ in 12 amino acids in gp160 – substitutions in both gp120 and gp41 reduced the ability of sCD4, IgG1b12, F105 and AG1121 to Env achieve saturation and full occupancy, and neutralize KU-1 – 17b and 2F5 also bound less efficiently to HXBc2P3.2, although 2G12 was able to bind both comparably [Si2001]
- 2F5: ELNKWA is an escape variant not recognized by the broadly neutralizing MAb 2F5, which recognizes the core epitope ELDKWA – Abs were raised against the peptide escape variant CGELNKWAGELNKWA linked to KLH carrier – these polyclonal antibodies, like the monoclonal antibody TH-Ab1 also raised to ELNKWA, could recognize ELDKWA and escape mutant peptide epitopes ELEKWA and ELDEWA [Dong2001]
- 2F5: Mutations in two glcosylation sites in the V2 region of HIV-1 ADA at positions 190 and 197 (187 DNTSYRLINCNTS 199) cause the virus to become CD4-independent and able to enter cells through CCR5 alone – these same mutations tended to increase the neutralization sensitivity of the virus, including to antibody 2F5 [Kolchinsky2001]
- 2F5: A peptide called 5-Helix was designed that binds to the C-peptide region of gp41 – 5-Helix is a potent inhibitor of HIV-1 entry that binds immediately COOH-terminal to the C-peptide region targeted by 5-Helix – the conformation of the bound 2F5 epitope is a hairpin turn [Root2001]
- 2F5: A phage peptide library was screened with MAb 2F5, and from the peptides that bound the amino acids DKW were found to be most critical for binding – the mimetic peptide RDWSFDRWSLSEFWL elicited a cross-reactive Ab response to gp41 when used to immunize rabbits [Tumanova2001]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 2F5: Abs against the V3 loop (50.1, 58.2, 59.1, 257-D, 268-D, 447-52D), CD4BS (IgG1b12, 559-64D, F105), CD4i (17b), and to gp41 (2F5, F240) each showed similar binding efficiency to Env derived from related pairs of primary and TCLA lines (primary: 168P and 320SI, and TCLA: 168C and 320SI-C3.3), but the TCLA lines were much more susceptible to neutralization suggesting that the change in TCLA lines that make them more susceptible to NAbs alters some step after binding [York2001]
- 2F5: This paper primarily concerns 4E10 and Z13, MAbs that both bind proximally to the 2F5 binding site to a conserved epitope, and that neutralize some primary isolates from clades B, C, and E – the minimal 2F5 epitope is determined to be EQELLELDKWASLW, based on screening a gp160 fragment expression library, longer than previous studies – broadly neutralizing MAbs 2F5, IgG1b12, and 4E10 and Z13 fail to neutralize different subsets of viruses [Zwick2001b]
- 2F5: Neutralization synergy between anti-HIV NAbs b12, 2G12, 2F5, and 4E10 was studied – a classic fixed-ratio method was used, as well as a method where one Ab was fixed at a low neutralization titer and the other was varied – using primary isolates, a two-four fold enhancement of neutralization was observed with MAb pairs, and a ten-fold enhancement with a quadruple Ab combination – no synergy was observed with any MAb pair in the neutralization of TCLA strain HXB2 [Zwick2001c]
- 2F5: Review of studies in macaques that have shown immune control of pathogenic SHIV viremia, improved clinical outcome, and protection, and the implications of the observations for HIV vaccines [Mascola2001]
- 2F5: SF162DeltaV2 is a virus that has a 30 amino acids deletion in the V2 loop that does not abrogate its infectivity but renders it highly susceptible to neutralization – when incorporated into a codon-optimized DNA vaccine with a CMV promoter and delivered by gene gun, SF162DeltaV2 gave higher neutralizing Ab titers against SF162 than did SF162 itself, and Abs that cross-neutralized non-homologous primary isolates were obtained only when SF162DeltaV2, but not intact SF162, was used as the immunogen – Control MAbs 2F5 and 2G12 could neutralize all of the following primary isolates: 91US056(R5), 92US714(R5), 92US660(R5), 92HT593(R5X4), and BZ167(R5X4), while after the first protein boost, the sera from two SF162DeltaV2 immunized macaques could neutralize 91US056(R5), 92US714(R5), 92US660(R5) and ADA(R5), but not 92HT593(R5X4) or 92US657(R5) – the pattern of cross-recognition shifted after the second boost [Barnett2001]
- 2F5: Moore and colleagues review the data concerning the lack of a clear relationship between genetic subtype and serotype – 2F5 is considered in some detail, as it represents a rare vulnerability from the neutralizing antibody perspective, although while it is apparently linear, attempts to present the peptide to the immune system have failed to elicit neutralizing Abs [Moore2001]
- 2F5: Neutralizing synergy between MAbs 1b12, 2G12 and 2F5 was studied using surface plasmon resonance to determine the binding kinetics for these three mAbs with respect to monomeric and oligomeric env protein gp160 IIIB – the 2G12 epitope is highly accessible on both monomeric and oligomeric Envs, 1b12 is highly accessible on monomers but not oligomers, and 2F5 on neither form – binding of 2G12 exposes the 2F5 epitope on gp160 oligomers [Zeder-Lutz2001]
- 2F5: Matrix-assisted laser desorption ionization mass spectrometry (MALDI-MS) in combination with proteolytic protection was used to identify the functional epitope for MAb 2F5, NEQELLELDKWASLWN, in the disulfide bond associated gp120/gp41 protein SOS-gp140 (JRFL) – this minimal epitope is much larger than the ELDKWA core epitope previously defined by peptide ELISA, and this could help explain why ELDKWA-peptides are poor immunogens in terms of eliciting a 2F5-like antibody response [Parker2001]
- 2F5: A luciferase-reporter gene-expressing T-cell line was developed to facilitate neutralization and drug-sensitivity assays – luciferase and p24 antigen neutralization titer end points were found comparable using NAb from sera from HIV+ donors, and MAbs 2F5, 2G12 and IgG1b12 [Spenlehauer2001]
- 2F5: A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6 – six gave significant neutralization at 2 to 10 ug/ml: 2F5, 50-69, IgG1b12, 447-52D, 2G12, and 670-D six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98-6, and 1281 – no synergy, only additive effects were seen for pairwise combinations of MAbs, and antagonism was noted between gp41 MAbs 50-69 and 98-6, as well as 98-6 and 2F5 [Verrier2001]
- 2F5: 4E10 binds proximal to 2F5 and neutralizes primary isolates of clades A, B, C, D, and E – viruses that were resistant to 2F5 were neutralized by 4E10 and vice versa [Stiegler2001]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 2F5: A combination of MAbs IgG1b12, 2F5, and 2G12 was given postnatally to four neonates macaques that were then challenged with highly pathogenic SHIV89.6P – one of the four infants remained uninfected after oral challenge, two infants had no or a delayed CD4(+) T-cell decline [Hofmann-Lehmann2001]
- 2F5: Twenty HIV clade C isolates from five different countries were susceptible to neutralization by anti-clade B MAbs in a synergistic quadruple combination of mAbs IgG1b12, 2G12, 2F5, and 4E10 [Xu2001]
- 2F5: Oligomeric gp140 (o-gp140) derived from R5 primary isolate US4 was characterized for use as a vaccine reagent – antigen capture ELISA was used to compare the antigenicity of gp120 and o-gp140 using a panel of well characterized MAbs – 2F5 recognized o-gp140 [Srivastava2002]
- 2F5: The fusion process was slowed by using a suboptimal temperature (31.5 C) to re-evaluate the potential of Abs targeting fusion intermediates to block HIV entry – preincubation of E/T cells at 31.5 C enabled polyclonal anti-N-HR Ab and anti-six-helix bundle Abs to inhibit fusion, indicating six-helix bundles form prior to fusion – the preincubation 31.5 C step did not alter the inhibitory activity of neutralizing Abs anti-gp41 2F5, or anti-gp120 2G12, IG1b12, 48d, and 17b [Golding2002b]
- 2F5: Ab binding characteristics of SOS gp140 were tested using SPR and RIPA – SOS gp140 is gp120-gp41 bound by a disulfide bond – NAbs 2G12, 2F5, IgG1b12, CD4 inducible 17b, and 19b bound to SOS gp140 better than uncleaved gp140 (gp140unc) and gp120 – non-neutralizing MAbs 2.2B (binds to gp41 in gp140unc) and 23A (binds gp120) did not bind SOS gp140 – SOS gp140-2F5-IgG1b12 formed multiple ring structures composed of two SOS gp140 proteins bridged by two Ab molecules, while 2F5 and 2G12 formed extended chains rather than closed rings [Schulke2002]
- 2F5: Expanding the minimal epitope ELDKWA to an end-capped, linear nonapeptide, Ac-LELDKWASL-amide attained maximal affinity within a set of native gp41-sequence peptides – scanning single residue substitutions confirmed that essential recognition requirements were the central DKW core sequence and the importance of the terminal Leu residues for high-affinity binding – high specificity binding pockets at central Lys and Trp side-chains and an absolute requirement for the carboxylate group of the Asp side chain were found – the nine residue fragment flanked by pairs of Ser and constrained by a disulfide bridge had high affinity for 2F5 [Tian2002]
- 2F5: ELDKWAS was embedded into a beta-turn-like conformational site on a framework of an antibody specific for human leukocyte antigen HLA-DR – this construct was recognized by 2F5, and is suggested as an adjuvant-independent vaccine candidate [Ho2002]
- 2F5: Passive immunization of neonate macaques with a combination of F105+2G12+2F5 conferred complete protection against oral challenge with SHIV-vpu+ or – the combination b12+2G12+2F5 conferred partial protection against SHIV89.6 – such combinations may be useful for prophylaxis at birth and against milk born transmission – the synergistic combination of IgG1b12, 2G12, 2F5, and 4E10 neutralized a collection of HIV clade C primary isolates [Xu2002]
- 2F5: A modified gp140 (gp140deltaCFI), with C-term mutations intended to mimic a fusion intermediate and stabilize trimer formation, retained antigenic conformational determinants as defined by binding to CD4 and to MAbs 2F5, 2G12, F105, and b12, and enhanced humoral immunity without diminishing the CTL response in mice injected with a DNA vaccine [Chakrabarti2002]
- 2F5: DP178 is a peptide derived from the C-term heptad repeat of gp41 that is a potent inhibitor of viral-mediated fusion—it contains the 2F5 epitope but fails to stimulate 2F5-like NAbs upon immunization—the peptide was extended to force an increase in helicity, and the modified peptide had a increase in affinity for 2F5, but upon guinea pig immunization although high peptide-specific Ab titers were achieved the sera were incapable of viral neutralization—the authors propose that 2F5 may bind with low affinity to a maturation intermediate, which may account for its breadth and why it is hard to recreate the epitope, but also suggests that the high concentrations required for neutralization are not relevant *in vivo* [Joyce2002].
- 2F5: Six sera from HIV-exposed uninfected individuals(EU) had IgA neutralizing activity dominated by recognition of a distinctive epitope within gp41, QARILAV – sera of QAFILAV-immunized BALB/c mice was neutralizing with the dose-dependent behavior similar to 2F5 [Clerici2002a]
- 2F5: A combination of MAbs 2F5 and 2G12 given in multiple infusions was found to be safe and well tolerated even in high doses in a phase I study of seven HIV-1 infected healthy volunteers—the median elimination half-life was 7.94 days for 2F5, and 16.48 for 2G12—no anti-2F5 or anti-2G12 IgM or IgG responses were detected—although there was some transient increases, overall plasma viral RNA levels decreased in 6/7 volunteers, by a median of 0.62 log_10 [Armbruster2002].

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 2F5: A series of mutational changes were introduced into the YU2 gp120 that favored different conformations – 375 S/W seems to favor a conformation of gp120 closer to the CD4-bound state, and is readily bound by sCD4 and CD4i MAbs (17b, 48d, 49e, 21c and 23e) but binding of anti-CD4BS MAbs (F105, 15e, IgG1b12, 21h and F91 was markedly reduced – IgG1b12 failed to neutralize this mutant, while neutralization by 2G12 was enhanced – 2F5 did not neutralize either WT or mutant, probably due to polymorphism in the YU2 epitope – another mutant, 423 I/P, disrupted the gp120 bridging sheet, favored a different conformation and did not bind CD4, CCR5, or CD4i antibodies, but did bind to CD4BS MAbs [Xiang2002b] • 2F5: HIV-1 gp160ΔCT (cytoplasmic tail-deleted) proteoliposomes (PLs) containing native, trimeric envelope glycoproteins from R5 strains YU2 and JRFL, and X4 strain HXBc2, were made in a physiologic membrane setting as candidate immunogens for HIV vaccines—2F5 bound to gp160ΔCT with a reconstituted membrane ten-fold better than the same protein on beads (except for the YU2 form that doesn't bind 2F5)—anti-CD4BS MAbs IgG1b12 and F105, A32 (C1-C4), C11 (C1-C5), and 39F (V3) MAbs bound gp160ΔCT PLs indistinguishably from gp160ΔCT expressed on the cell surface [Grundner2002]. • 2F5: Rhesus macaques were better protected from vaginal challenge with SHIV89.6D (MAb 2G12, 2/4; MAbs 2F5/2G12, 2/5; and HIVIG/2F5/2G12, 4/5 infected) than from intravenous challenge (MAb 2G12, 0/3; MAbs 2F5/2G12, 1/3; and HIVIG/2F5/2G12, 3/6 infected)– the animals that were infected by vaginal challenge after Ab infusion had low or undetectable viral RNA levels and modest CD4 T-cell decline [Mascola2002] • 2F5: A 2F5 anti-idiotype murine MAb Ab2/3H6 was developed that blocks 2F5 binding to a synthetic epitope peptide and to gp160 in an ELISA competition assay – Ab2/3H6 diminished the neutralizing potency of 2F5 – Ab2/3H6 Fab fragments were capable of inducing neutralizing Abs and 2F5-epitope specific responses in immunized B6D2F1 mice [Kunert2002] • 2F5: Review of NAbs that notes that 2F5 alone or in combination with other MAbs can protect some macaques against SHIV infection, that it is safe and well tolerated in humans, and that illustrates gp41's conformational change and exposure of the 2F5 epitope in the transient pre-hairpin form [Ferrantelli2002] • 2F5: Review of NAbs that discusses mechanisms of neutralization, passive transfer of NAbs and protection in animal studies, and vaccine strategies [Liu2002] • 2F5: UK Medical Research Council AIDS reagent: ARP3063 • 2F5: NIH AIDS Research and Reference Reagent Program: 1475					
668	polyclonal	gp160 (662–667)	gp41 (662–667)	ELDKWA	no	Vaccine	guinea pig
		Vaccine *HIV component:* gp41 peptide **References** Joyce2002 • 2F5: DP178 is a peptide derived from the C-term heptad repeat of gp41 that is a potent inhibitor of viral-mediated fusion – it contains ELDKWA but fails to stimulate 2F5-like NAbs upon immunization – the peptide was extended to force an increase in helicity, and the modified peptide had a increase in affinity for 2F5, but upon guinea pig immunization although high peptide-specific Ab titers were achieved the sera were incapable of viral neutralization – the authors propose that 2F5 may be a low affinity maturation intermediate, which may account for its breadth and why it is hard to recreate the NAb response, but also suggests that the high concentrations required for neutralization are not relevant in vivo [Joyce2002]					
669	5B2	gp160 (662–667)	Env (669–674 IIIB)	ELDKWA		Vaccine	murine (IgG)
		Vaccine *Vector/Type:* peptide keyhole limpet hemocyanin (KLH) conjugate *Strain:* IIIB *HIV component:* gp41 **Ab type** C-domain **References** Tian2001 • 5B2: There is an RT specific Ab [Szilvay1992] and a gp41 specific Ab [Tian2001] both called 5B2 • 5B2: Peptides GPGRAFY and ELDKWA were conjugated to keyhole limpet hemocyanin and used to raise mouse MAbs – MAb hybridomas were generated with defined specificity – 5B2 and 9G11 bind to the peptide and to rgp41 [Tian2001]					
670	9G11	gp160 (662–667)	Env (669–674 IIIB)	ELDKWA		Vaccine	murine (IgG)
		Vaccine *Vector/Type:* peptide keyhole limpet hemocyanin (KLH) conjugate *Strain:* IIIB *HIV component:* gp41					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		Ab type C-domain **References** Tian2001 • 9G11: Peptides GPGRAFY and ELDKWA were conjugated to KLH and used to raise mouse monoclonal Ab—MAb hybridomas were generated with defined specificity—5B2 and 9G11 bind to the peptide and to rgp41 [Tian2001].					
671	TH-Ab1	gp160 (662–667)	gp41 (669–674)	ELNKWA	L P	Vaccine	rabbit (IgG1)
		Vaccine *Vector/Type:* peptide keyhole limpet hemocyanin (KLH) conjugate *Strain:* B clade TH936705 *HIV component:* gp41 *Adjuvant:* Freund's adjuvant **Ab type** C-domain **References** Xiao2000a, Dong2001 • TH-Ab1: ELNKWA is an escape variant not recognized by the broadly neutralizing MAb 2F5, which recognizes the core epitope ELDKWA—Abs were raised against the peptide escape variant CGELNKWAGELNKWA linked to KLH carrier—these polyclonal antibodies, like the MAb TH-Ab1 also raised to ELNKWA, could recognize ELDKWA and escape mutant peptide epitopes ELEKWA and ELDEWA [Dong2001].					
672	polyclonal	gp160 (662–667)	gp41	ELDKWA	L P	Vaccine	rabbit
		Vaccine *Vector/Type:* peptide *HIV component:* gp41 **Ab type** C-domain **References** Liao2000 • Low levels of anti-ELDKWA antibodies are observed in HIV-1+ individuals, so a C-domain P2 peptide linked to a carrier was used to immunize mice and rabbits, and stimulated a high-level anti-ELDKWA response in mice and rabbits – vaccine was C-TSLIHSLIEESQNQQEKNEQELLELDKWA linked to carrier peptide K/G [(KGGG)_7-K] [Liao2000]					
673	polyclonal	gp160 (662–667)	gp41 (669–674)	ELDKWA		Vaccine	murine, rabbit
		Vaccine *Vector/Type:* peptide *HIV component:* Env *Adjuvant:* BSA **Ab type** C-domain **References** Xiao2000b • Strong epitope-specific neutralizing antibody responses were induced using a Env peptide bound to BSA, C(ELDKWAG)_4-BSA, but not full gp160 [Xiao2000b]					
674	polyclonal	gp160 (662–667)	gp41 (662–667 BH10)	ELDKWA	L	Vaccine	murine (IgG, IgA)
		Vaccine *Vector/Type:* influenza *Strain:* BH10 *HIV component:* gp41 peptide **Ab type** C-domain **References** Muster1994, Muster1995 • Sustained ELDKWA specific IgA response in mucosa of immunized mice [Muster1995]					
675	polyclonal	gp160 (662–667)	gp120 (669–674)	ELDKWA		Vaccine	rabbit (Ig)
		Vaccine *Vector/Type:* polyepitope, protein *HIV component:* gp160 *Adjuvant:* BSA **Ab type** C-domain **References** Lu2000c, Lu2000b • High titer response to ELDKWA and RILAVERYLKD was observed upon vaccination with multiple-epitope vaccine CG-GPGRAFY-G-ELDKWA-G-RILAVERYLKD conjugated to BSA, with a weak response to GPGRAFY – immunization with CG-(ELDKWA-GPGRAFY)_2-K was also tried, yielding a strong Ab response to both ELDKWA and GPGRAFY – gp160 vaccination yielded strong Ab response but not to any of the peptides studied here [Lu2000c, Lu2000b]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
676	4E10	gp160 (671–676)	gp160 (671–676 MN)	NWFDIT	P	HIV-1 infection	human (IgG3κ)

Donor Herman Katinger, Inst. Appl. Microbiol. University of Agricultural Science, Vienna, Austria
References Buchacher1992, Buchacher1994, D'Souza1994, Stiegler2001, Zwick2001b, Zwick2001c, Xu2001, Xu2002, Ferrantelli2002

- 4E10: MAbs generated by hybridoma, electrofusion of PBL from HIV-1+ volunteers with CB-F7 heteromyeloma cells – also binds to MHC class II proteins – anti-class II Abs are only found in HIV-1 positive people – this paper maps 4E10's binding site to AEGTDRV, gp160(823-829), but the later Zwick et al. study in 2001 revised the epitope location [Buchacher1994]
- 4E10: Included in a multi-lab study for antibody characterization, binding and neutralization assay comparison [D'Souza1994]
- 4E10: 4E10 binds proximal to 2F5 and neutralizes primary isolates of clades A, B, C, D, and E – viruses that were resistant to 2F5 were neutralized by 4E10 and vice versa [Stiegler2001]
- 4E10: MAbs 4E10 and Z13 both bind proximally to 2F5 to a conserved linear epitope that has some conformational aspects – both bind to MN virions, bind weakly to infected cells in a manner that is not disrupted by sCD4 and neutralize some primary isolates from clades B, C, and E – maps minimal 4E10 epitope to NWFDIT, contrary to an earlier report – different strains were refractive to neutralization by broadly neutralizing Abs IgG1b12, 2F5, Z13 and 4E10 [Zwick2001b]
- 4E10: Neutralization synergy between anti-HIV NAbs b12, 2G12, 2F5, and 4E10 was studied – a classic fixed-ratio method was used, as well as a method where one Ab was fixed at a low neutralization titer and the other was varied – using primary isolates, a two-four fold enhancement of neutralization was observed with MAb pairs, and a ten-fold enhancement with a quadruple Ab combination – no synergy was observed with any MAb pair in the neutralization of TCLA strain HXB2 [Zwick2001c]
- 4E10: Twenty HIV clade C isolates from five different countries were susceptible to neutralization by anti-clade B MAbs in a synergistic quadruple combination of mAbs IgG1b12, 2G12, 2F5, and 4E10 [Xu2001]
- 4E10: Passive immunization of neonate macaques with a combination of F105+2G12+2F5 conferred complete protection against oral challenge with SHIV-vpu+ —the combination b12+2G12+2F5 conferred partial protection against SHIV89.6—such combinations may be useful for prophylaxis at birth and against milk born transmission—the synergistic combination of IgG1b12, 2G12, 2F5, and 4E10 neutralized a collection of HIV clade C primary isolates [Xu2002].
- 4E10: Review of NAbs illustrating gp41's conformational change and exposure of the 4E10/Z13 epitope in the transient pre-hairpin form [Ferrantelli2002]

677	Z13	gp160 (671–676)	gp41 (671–676 MN)	NWFDIT	P	HIV-1 infection	human (IgG1κ)

Ab type C-term
References Zwick2001b, Ferrantelli2002

- Z13: MAb 4E10 and FAb Z13 both bind proximally to 2F5 to a relatively conserved linear epitope that has some conformational aspects – both bind to MN virions, bind weakly to infected cells in a manner that is not disrupted by sCD4 and can neutralize some primary isolates from clades B, C, and E – Z13 was selected using a phage display library with the MN gp41 peptide LLELDKWASLWNWFDITNWSW from an HIV infected donor who had an exceptionally broad NAb response – different strains were refractive to neutralization by broadly neutralizing Abs IgG1b12, 2F5, Z13 and 4E10 – epitope location noted here is by analogy to MAb 4E10 [Zwick2001b]
- Z13: Review of NAbs that notes Z13 is a phage display generated FAb fragment from a B clade infected individual and that illustrates gp41's conformational change and exposure of the 4E10/Z13 epitope in the transient pre-hairpin form [Ferrantelli2002]

678	B30	gp160 (720–734)	gp41 (720–734 BH10)	HLPIPRGPDRPEGIE		Vaccine	murine (IgG1)

Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* gp160
Donor George Lewis
References Abacioglu1994

- B30: Epitope boundaries mapped by peptide scanning [Abacioglu1994]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
679	polyclonal	gp160 (724–745)	gp41 (731–752)	PRGPDRPEGIEEEGGERDRDRS		Vaccine	murine (IgA, IgG2a)

Vaccine *Vector/Type:* Cowpea mosaic virus *Strain:* IIIB *HIV component:* gp41 peptide
References Durrani1998

- Comparison of intranasal and oral immunization of HIV-1 peptide expressed in a plant viral vector – intranasal gave the better response [Durrani1998]

680	41S-2	gp160 (725–745)	gp160 (732–750)	RGPDRPEGIEEEGGERDRDRS	yes	Vaccine	murine (IgG2bκ)

Vaccine *Vector/Type:* peptide keyhole limpet hemocyanin (KLH) conjugate *HIV component:* gp41
References Hifumi2000

- 41S-2: BALBc mice were immunized with gp41 peptide and a MAb specific for the peptide was generated – isolated MAb light chains displayed proteolytic activity toward the peptide epitope which may be due to a catalytic triad on light chain (Asp73, Ser76, and His79) – no catalytic activity was observed for the whole antibody [Hifumi2000]

681	447-52D (447/52-DII, 447-52-D, 447d, 447-52-D, 447-D, 447, 447D)	gp160 (726–729)	gp120 (MN)	GPXR	L	HIV-1 infection	human (IgG3λ)

Ab type V3 **Donor** Dr. Susan Zolla-Pazner, NYU Med Center NY, NY, or Cellular Products Inc, Buffalo, NY, USA
References Gorny1992, Buchbinder1992, Karwowska1992b, Gorny1993, Keller1993, Cavacini1993a, Spear1993, Conley1994a, Laal1994, VanCott1994, Gorny1994, Moore1994a, Sattentau1995a, Fontenot1995, Saarloos1995, Zolla-Pazner1995a, Zolla-Pazner1995b, Moore1995a, Moore1995b, Forthal1995, Jagodzinski1996, Trkola1996a, Sattentau1996, D'Souza1997, Binley1997a, Fouts1997, Hioe1997a, Hioe1997b, Boots1997, Parren1997c, Hill1997, Gorny1997, Inouye1998, Mondor1998, Smith1998, Parren1998a, Zolla-Pazner1999a, Zolla-Pazner1999b, Connor1998, Gorny1998, Nyambi1998, Hioe1999, Beddows1999, Gorny2000a, Grovit-Ferbas2000, Hioe2000, Ly2000, Nyambi2000, Park2000, York2001, Verrier2001, Srivastava2002, Sharon2002, Gorny2002, He2002, Ferrantelli2002, Poignard2003

- 447-52D: Requires GPXR at the tip of the V3 loop – neutralizes a broad array of B clade lab isolates [Gorny1992]
- 447-52D: 60-fold increase in neutralization potency when combined 1:1 with human MAb 588-D [Buchbinder1992]
- 447-52D: Reacts with MN, NY5, CDC4, SF2, RF, WM52, and HXB2 [Karwowska1992b]
- 447-52D: Neutralizes MN and IIIB: GPGR, and binds SF2: GPGR [Gorny1993]
- 447-52D: Peptide phage library showed that any of the residues ADGLMNQRS in the X position tolerated in peptides that react well with the antibody [Keller1993]
- 447-52D: Additive neutralization of MN and SF2 when combined with CD4 binding site MAb F105 – supra-additive neutralization of RF [Cavacini1993a]
- 447-52D: Complement mediated virolysis of IIIB, but not in the presence of sCD4 [Spear1993]
- 447-52D: Requires GPxR at the tip of the V3 loop, common in B clade – neutralized primary isolates [Conley1994a]
- 447-52D: Neutralization synergy in combination with CD4 binding domain MAbs [Laal1994]
- 447-52D: GPGQ in MAL resulted in enhanced dissociation – GPGQ in CM234 or K14T did not bind – binding affected by identity of amino acids flanking GPGR core [VanCott1994]
- 447-52D: Mild oxidation of carbohydrate moieties does not alter binding [Gorny1994]
- 447-52D: Competition studies with human sera from seroconverting individuals showed that anti-CD4 BS antibodies can arise very early in infection, comparable or prior to anti-V3 antibodies [Moore1994a]
- 447-52D: Called 447d – Formalin inactivation of virus at 0.1% formalin for 10 hours at 4 degrees was optimal for inactivation of virus while maintaining epitope integrity [Sattentau1995c]
- 447-52D: Called 447 – The tip of the V3 loop was presented in a mucin backbone – higher valency correlates with stronger affinity constant [Fontenot1995]
- 447-52D: Ab-mediated activation of complement on HIV+ cells is higher than Ab independent activation—what has been termed "Ab independent" in fact results in part from IgM in normal human serum that is HIV-cross-reactive [Saarloos1995]
- 447-52D: Serotyping study using flow-cytometry – bound only to GPGR V3 loop tips [Zolla-Pazner1995a]
- 447-52D: Neutralization of primary and prototype laboratory HIV-1 isolates using a resting cell assay enhances sensitivity [Zolla-Pazner1995b]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 447-52D: Binding affected by identity of amino acids flanking GPGR core – poor breadth of primary virus neutralization [Moore1995a]
- 447-52D: Review: the V3 loop motif GPGR is not common outside subtype B isolates, MAb 19b is more cross-reactive [Moore1995b]
- 447-52D: Neutralizing (- complement), no ADCC activity, and no viral enhancing activity [Forthal1995]
- 447-52D: Called 447-52-D – The sulfated polysaccharide curdlan sulfate (CRDS) binds to the Envelope of T-tropic viruses and neutralizes virus – CRDS inhibits binding [Jagodzinski1996]
- 447-52D: Neutralizes JR-FL – strongly inhibits gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study [Trkola1996a]
- 447-52D: Review: called 447-52-D – only four epitopes have been described which can stimulate a useful neutralizing response to a broad spectrum of primary isolates, represented by the binding sites of MAbs: 447-52-D, 2G12, Fab b12, and 2F5 [Sattentau1996]
- 447-52D: In a multilaboratory blinded study, failed to consistently neutralize any of nine B clade primary isolates – many of these isolates had the GPGR motif at the apex of the V3 loop [D'Souza1997]
- 447-52D: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric Env binding – 447-52D bound monomer, oligomer, and neutralized JRFL [Fouts1997]
- 447-52D: Tested using a resting cell neutralization assay [Hioe1997a]
- 447-52D: Four primary isolates showed distinct patterns of sensitivity to neutralization by polyclonal sera or plasma and MAbs – BZ167 was the only isolate inhibited by all polyclonal sera and plasma tested, and was also neutralized by 8/17 MAbs, in particular anti-V3 loop (419-D, 447-52D, 782-D, and 838-D), anti-CD4bd (559/64-D, 654-D and 830-D and a cluster II of gp41 directed MAb (98-6) – isolates 92HT593 and 91US056 were neutralized by V3 loop (419-D, and 447-52D)and cluster II gp41 (98-6) MAbs at higher concentrations – US4 was neutralized by some of the polyclonal sera/plasma tested and not at all by MAbs individually or by a cocktail of ten MAbs consisting of 419-D, 447-52D, 782-D, 838-D, 559/64-D, 654-D, 450-D, 670-D, 1281-D and 98-6 [Hioe1997b]
- 447-52D: Viral binding inhibition by 447-D was correlated with neutralization (all other neutralizing MAbs tested showed some correlation except 2F5) [Ugolini1997]
- 447-52D: Neutralizes TCLA strains but not primary isolates [Parren1997c]
- 447-52D: Called 447 – gp120 can inhibit MIP-1alpha from binding to CCR5, but this inhibitory effect is blocked by pre-incubation of gp120 with three anti-V3 MAbs: 447, 257, 1027 – MAb 670 which binds in the C5 region had no effect [Hill1997]
- 447-52D: Abs that recognize discontinuous epitopes can identify mimotopes from a phage peptide display library – 447-52D has an epitope involving the tip of the V3 loop, that was previously studied with this method [Keller1993] – in Keller et al., with no competition, LxGPxR was the most common six-mer, 38% of the peptides – after competition with a gp120 IIIB ligand (QRGPGR)i, RGPxR was the most common and one peptide had the sequence QRGPGR, showing type specific mimotopes can be enriched by strain specific ligand competition protocols [Boots1997]
- 447-52D: Used as a control for comparison to five V3 RF selected antibodies – 447-52D was reactive with A, B, and C clade peptides, but not E [Gorny1997]
- 447-52D: Called 447-D – 447-D resistance took longer to acquire in virus with the M184V substituted RT, and had the form (AAC N to TAC Y) at position 5 of the V3 loop, rather than the GPGR to GPGR resistance found with wildtype RT [Inouye1998]
- 447-52D: Inhibits binding of Hx10 to both CD4 positive and negative HeLa cells [Mondor1998]
- 447-52D: Called 447-52-D – The tip of the MN V3 loop was inserted into cold causing human rhinovirus 14 (HRV14) – chimeras were immunoselected, and chimeric viruses were neutralized by anti-V3 loop antibodies, and 447-52D was among the Abs used – chimeric viruses elicited potent NAbs in guinea pigs against ALA-1 and MN [Smith1998]
- 447-52D: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren1998a]
- 447-52D: Ab from gp120 vaccinated individuals prior to infection, who subsequently became HIV infected, could not achieve 90% neutralization of the primary virus by which the individuals were ultimately infected – these viruses were not particularly refractive to neutralization, as determined by their susceptibility to neutralization by MAbs 2G12, IgG1b12, 2F5 and 447-52D [Connor1998]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 447-52D: Kinetic parameters were measured, and the association rates were similar, but dissociation rate constants were quite variable for V3 MAbs, 1324E was comparable to 447-52D [Gorny1998]
- 447-52D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – 447-52D was the most potent and cross-reactive of 18 human MAbs tested and was the only MAb which bound to virions from isolates CA20 (subtype F), CA13 (subtype H), and VI526 (subtype G) [Nyambi1998]
- 447-52D: Review of clade specificity and anti-V3 HIV-1-Abs [Zolla-Pazner1999a]
- 447-52D: MAb peptide-reactivity pattern clustered with the immunological related MAbs: 1334, 419, 504, 447, 453 and 537 – the core amino acids GP tended to be critical for reactivity in this group – 447 reacted with peptides containing GPGR, but also with many lacking this sequence (GPGQ, for example), and it failed to react with 2/14 peptides containing GPGR, illustrating the importance of context [Zolla-Pazner1999b]
- 447-52D: The presence of leukocyte function-associated molecule 1 (LFA-1) promotes virus infectivity and hinders neutralization, and anti-LFA-1 MAbs can enhance the neutralizing effect of anti-HIV V3 MAb 447-52D and anti-HIV CD4BS MAb IgG1b12 – non-neutralizing anti-HIV CD4BS MAb 654-D did not become neutralizing in the presence of anti-LFA-1 MAbs [Hioe1999]
- 447-52D: rgp120 derived from a R5X4 subtype B virus, HIV-1 W61D, was used to vaccinate healthy volunteers and the resulting sera were compared with sera from HIV-1 positive subjects and neutralizing MAbs – TCLA strains showed enhanced 447-52D neutralization sensitivity relative to PBMC-adapted lines (32X increase between HIV-1(M2424/PBMC(p0)) and HIV-1(M2424/H9(p9)) and a >128X increase between HIV-1(W61D/PBMC) and HIV-1(W61D/SupT1) isolates) [Beddows1999]
- 447-52D: Binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – V3 MAbs 447-52D, 838-D, and 1334 bound with a 7-10 fold preference for the oligomer [Gorny2000a]
- 447-52D: To determine the antigenicity of virus killed by thermal and chemical inactivation, retention of conformation-dependent neutralization epitopes was examined, and exposure of CD4BS epitopes was found to be enhanced (MAbs IgG1b12, 205-46-9, and 205-43-1) – binding to 2G12 and 447-52D epitopes was essentially unaltered – the 17b CD4i epitope was also exposed [Grovit-Ferbas2000]
- 447-52D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – CD4BS MAbs or serum Ig from HIV+ individuals inhibited proliferative responses of gp120 specific T cells – V3 MAbs 447-52-D and 268-10-D did not effect proliferation [Hioe2000]
- 447-52D: Called 447D – SF162 is a neutralization-resistant HIV-1 isolate – N-linked glycosylation modifications in the V2 loop of the SF162 gp120 revealed that these sites prevent neutralization by CD4BS MAbs (IgG1b12 and IgGCD4), and protect against neutralization by V3 MAbs (447D and 391-95D) – V2-region glycosylation site mutations did not alter neutralization resistance to V2 MAbs (G3.4 and G3.136) or CD4i MAbs (17b and 48d) – V2 glycosylation site modification allows infection of macrophages, probably due to glycosylated forms requiring fewer CCR5 molecules for viral entry [Ly2000]
- 447-52D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 447-52D showed the highest cross-reactivity, bound to 24/26 viruses tested, but achieved 90% neutralization only against MN, 50% against CA5, and no neutralization was observed for 3 other isolates tested [Nyambi2000]
- 447-52D: Six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20-100 fold more efficient at neutralizing the sensitive form – the mutation L544P reduced binding of all MAbs against gp120 by causing conformational changes [Park2000]
- 447-52D: Abs against the V3 loop (50.1, 58.2, 59.1, 257-D, 268-D, 447-52D), CD4BS (IgG1b12, 559-64D, F105), CD4i (17b), and to gp41 (2F5, F240) each showed similar binding efficiency to Env derived from related pairs of primary and TCLA lines (primary: 168P and 320SI, and TCLA: 168C and 320SI-C3.3), but the TCLA lines were much more susceptible to neutralization suggesting that the change in TCLA lines that make them more susceptible to NAbs alters some step after binding – the dissociation constant, Kd of 447-52D for the cell associated primary and TCLA Envs was equal, 3nM [York2001]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 447-52D: A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6 – six gave significant neutralization at 2 to 10 ug/ml: 2F5, 50-69, IgG1b12, 447-52D, 2G12, and 670-D six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98-6, and 1281 – no synergy, only additive effects were seen for pairwise combinations of MAbs, and antagonism was noted between gp41 MAbs 50-69 and 98-6, as well as 98-6 and 2F5 [Verrier2001]
- 447-52D: Oligomeric gp140 (o-gp140) derived from R5 primary isolate US4 was characterized for use as a vaccine reagent—antigen capture ELISA was used to compare the antigenicity of gp120 and o-gp140 using a panel of well characterized MAbs—447-D recognized the gp120 monomer much more readily than o-gp140, suggesting the V3 loop is less exposed on o-gp140 than it is on the intact virions [Srivastava2002].
- 447-52D: The feasibility of determining the NMR structure of the V3(MN) peptide bound to the 447-52D Fab fragment was tested and a general strategy for obtaining NMR structures of V3 peptide-Fab fragments developed – preliminary NMR spectra for 447-52D complexed to a 23 amino acid V3 peptide was obtained [Sharon2002]
- 447-52D: Conformation-dependent anti-V3 loop Abs may be more cross-reactive, so six new V3 MAbs were generated – the six new MAbs all bind to the tip of the V3 loop and cross-compete with the MAb 447-52D and are conformationally sensitive – MAbs showed cross-clade binding to native, intact virions of clades A(N=2), B(N=4), and F(N=2), limited binding to C(N=3) and D(N=3), and did not bind to CRF01(subtype E, N=2) – the strength binding was highly correlated with percent neutralization using the ghost cell or PHA blast assay – five well-characterized MAbs were used as controls: anti-V3 447-52D (anti-V3 MAb for competition and neutralization studies), 654 (anti-CD4BS used as a conformation-sensitive MAb control), 1331A (anti-C5 used as a linear binding site MAb control), MAb 246 (anti-gp41 MAb that bound to primary isolates of all clades) – 447-52D bound to primary isolates from all clades except CRF01 (E), was conformationally sensitive and showed the some of the most potent neutralizing activity [Gorny2002]
- 447-52D: Transgenic mice carrying human genes allowing production of fully human MAbs were used to rapidly create a panel of anti-HIV gp120 MAb producing hybridomas by immunization with HIV SF162 gp120 – the previously described human MAbs 5145A(CD4BS) , 4117C (plus others, V3) and 697D (and SC258, V2) were used as controls [He2002]
- 447-52D: Review of NAbs [Ferrantelli2002]
- 447-52D: Virion capture assays are not a good preditor of neutralization, and the presentation of epitopes using this assay seems to be different from that of functional Envelope spikes on primary isolates – F105 and b6 could efficiently block the b12-mediated capture of infectious virions in a virus capture, but did not inhibit b12 neutralization – Ab 447-52D was able to potently neutralize 89.6 and to neutralize JR-CSF at a high concentration but poorly neutralized ADA – b12 was potent at neutralizing the three primary virions JR-CSF, ADA, and 89.6, but anti-V3 Abs 447-52D and 19b, which did not neutralize JR-CSF and ADA, captured amounts of p24 equal to or higher than the amounts captured by the neutralizing Ab b12 [Poignard2003]

682 C8 gp160 (727–732) gp41 (727–732 BH10) PDRPEG no Vaccine murine (IgG1)

Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* gp160

References Pincus1993a, Pincus1993b, Abacioglu1994, McLain2001

- C8: Immunotoxin of C8 coupled to ricin-A does not mediate cells killing, and is not affected by sCD4 [Pincus1993a]
- C8: Ab response in IIIB lab workers was compared to gp160 LAI vaccine recipients – C8 was used as a control – the dominant response among vaccinees was to this mid-gp41 region, but not among the infected lab workers – Abs binding this region do not neutralize, bind to infected cells, nor serve as immunotoxins [Pincus1993b]
- C8: Epitope boundaries mapped by peptide scanning [Abacioglu1994]
- C8: The substitution 725 RG (P[R–>G]GPDRPEGIEEEGGERDRDRS) alters the antigenic exposure of this region on the virion resulting in the loss of the downstream neutralizing epitope ERDRD, increased exposure of the epitope GPDRPEG in the virion, while the epitope IEEE remains unchanged [McLain2001]

683 B31 gp160 (727–734) gp41 (727–734 BH10) PDRPEGIE Vaccine murine (IgG1)

Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* gp160

References Abacioglu1994

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• B31: Epitope boundaries mapped by peptide scanning [Abacioglu1994]					
684	B33	gp160 (727–734)	gp41 (727–734 BH10)	PDRPEGIE	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *Strain:* NL43 *HIV component:* gp160 **References** Abacioglu1994, Bristow1994 • B33: There are two MAbs in the literature named B33, see also gp120, positions 123-142 – MAb generated in a study of the humoral immune response to Baculovirus-expressed mis-folded rgp160 IIIB:NL43, MicroGenSys [Bristow1994] • B33: Epitope boundaries mapped by peptide scanning IgG1 [Abacioglu1994]					
685	1576	gp160 (728–745)	gp41 (735–752 IIIB)	DRPEGIEEEGGERDRDRS	no	Vaccine	murine
		Vaccine *Vector/Type:* poliovirus *Strain:* IIIB *HIV component:* gp41 peptide **References** Vella1993 • 1576: Not neutralizing [Vella1993]					
686	1578	gp160 (728–745)	gp41 (735–752 IIIB)	DRPEGIEEEGGERDRDRS	no	Vaccine	murine
		Vaccine *Vector/Type:* poliovirus *Strain:* IIIB *HIV component:* gp41 peptide **References** Evans1989, Vella1993 • 1578: No neutralizing activity – epitope may be formed by regions from both poliovirus and HIV [Evans1989] • 1578: Core epitope: IEEE – in this study, neutralized IIIB, but not RF or MN [Vella1993]					
687	1579	gp160 (728–745)	gp41 (735–752 IIIB)	DRPEGIEEEGGERDRDRS	no	Vaccine	murine
		Vaccine *Vector/Type:* poliovirus *Strain:* IIIB *HIV component:* gp41 peptide **References** Vella1993 • 1579: Core epitope: IEEE – neutralized IIIB, but not RF or MN [Vella1993]					
688	1583	gp160 (728–745)	gp41 (735–752 IIIB)	DRPEGIEEEGGERDRDRS	no	Vaccine	murine
		Vaccine *Vector/Type:* poliovirus *Strain:* IIIB *HIV component:* gp41 peptide **References** Evans1989, Vella1993, Sattentau1995c • 1583: Neutralizing activity, less broad than 1577 [Evans1989] • 1583: Core epitope: ERDRD – Could neutralize HIV IIIB but not HIV RF [Vella1993] • 1583: Cytoplasmic domain, epitope not exposed at the surface of HIV-1 infected cells [Sattentau1995c]					
689	1899	gp160 (728–745)	gp41 (735–752 IIIB)	DRPEGIEEEGGERDRDRS	no	Vaccine	murine
		Vaccine *Vector/Type:* poliovirus *Strain:* IIIB *HIV component:* gp41 peptide **References** Vella1993 • 1899: Could neutralize HIV IIIB and HIV RF [Vella1993]					
690	1907	gp160 (728–745)	gp41 (735–752 IIIB)	DRPEGIEEEGGERDRDRS	no	Vaccine	murine
		Vaccine *Vector/Type:* poliovirus *Strain:* IIIB *HIV component:* gp41 peptide **References** Vella1993 • 1907: Could not neutralize HIV IIIB, RF or MN [Vella1993]					
691	1908	gp160 (728–745)	gp41 (735–752 IIIB)	DRPEGIEEEGGERDRDRS	no	Vaccine	murine
		Vaccine *Vector/Type:* poliovirus *Strain:* IIIB *HIV component:* gp41 peptide **References** Evans1989, Vella1993, Sattentau1995c • 1908: Neutralized IIIB, but not RF or MN [Vella1993]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 1908: Cytoplasmic domain, epitope not exposed at the surface of HIV-1 infected cells [Sattentau1995c]					
692	1909	gp160 (728–745)	gp41 (735–752 IIIB)	DRPEGIEEEGGERDRDRS	no	Vaccine	murine
		Vaccine *Vector/Type:* poliovirus *Strain:* IIIB *HIV component:* gp41 peptide **References** Vella1993 • 1909: Neutralized HIV IIIB but not HIV RF [Vella1993]					
693	41-1	gp160 (728–745)	gp41 (735–752 IIIB)	DRPEGIEEEGGERDRDRS	no	Vaccine	murine (IgMκ)
		Vaccine *Vector/Type:* peptide *Strain:* IIIB *HIV component:* gp41 peptide **References** Mani1994, Dalgleish1988 • 41-1: This antibody gp41(735-752 IIIB) [Dalgleish1988] seems to have been named the same as a different MAb to gp41(584-609) [Mani1994] • 41-1: Neutralizes HIV-1 but not HIV-2 strains [Dalgleish1988]					
694	41-2	gp160 (728–745)	gp41 (735–752 IIIB)	DRPEGIEEEGGERDRDRS	no	Vaccine	murine (IgMκ)
		Vaccine *Vector/Type:* peptide *Strain:* IIIB *HIV component:* gp41 peptide **References** Dalgleish1988 • 41-2: Neutralizes HIV-1 but not HIV-2 strains [Dalgleish1988]					
695	41-3	gp160 (728–745)	gp41 (735–752 IIIB)	DRPEGIEEEGGERDRDRS	no	Vaccine	murine (IgMκ)
		Vaccine *Vector/Type:* peptide *Strain:* IIIB *HIV component:* gp41 peptide **References** Dalgleish1988 • 41-3: Neutralizes HIV-1 but not HIV-2 strains [Dalgleish1988]					
696	ED6	gp160 (728–745)	gp41 (735–752 IIIB)	DRPEGIEEEGGERDRDRS	no		murine (IgM)
		References Evans1989					
697	LA9 (121-134)	gp160 (728–745)	gp41 (735–752 IIIB)	DRPEGIEEEGGERDRDRS	no		murine (IgM)
		References Evans1989					
698	1575	gp160 (728–745)	gp41 (735–752 IIIB)	DRPEGIEEEGGERDRDRS	no	Vaccine	murine
		Vaccine *Vector/Type:* poliovirus *Strain:* IIIB *HIV component:* gp41 peptide **Ab type** C-term **Donor** C. Vella, NIBSC, Potters Bar UK **References** Evans1989, Vella1993, Buratti1997, Cleveland2000a • 1575: Neutralizing activity, less broad than 1577 [Evans1989] • 1575: Core epitope: IEEE – neutralized IIIB, but not RF or MN [Vella1993] • 1575: Study shows that MAb 1575 can recognize the IEEE sequence in both gp41, and in the HPG30 region of the p17 protein – motif is conserved in both regions in different HIV-1 clades [Buratti1997] • 1575: Ab binding to IEEE suppresses neutralizing Ab binding to adjacent epitope ERDRD [Cleveland2000a]					
699	88-158/02	gp160 (732–747)	gp41 (732–752 IIIB)	GIEEEGGERDRDRSIR		Vaccine	murine (IgG2b)
		Vaccine *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* gp41 **References** Niedrig1992a • 88-158/02: Mild inhibition of in vitro activity at high MAb concentrations – profound enhancing activity at low concentrations – significant reactivity to virion – domain non-immunogenic in humans [Niedrig1992a]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
700	88-158/022	gp160 (732–747)	gp41 (732–752 IIIB)	GIEEEGGERDRDRSIR		Vaccine	murine (IgG2b)
		Vaccine *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* gp41 **References** Niedrig1992a • 88-158/022: Mild inhibition of in vitro activity at high MAb concentrations – profound enhancing activity at low concentrations – significant reactivity to virion – domain non-immunogenic in humans [Niedrig1992a]				
701	88-158/079	gp160 (732–747)	gp41 (732–752 IIIB)	GIEEEGGERDRDRSIR		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* gp41 **References** Niedrig1992a • 88-158/079: Mild inhibition of HIV in vitro at high MAb concentrations – profound enhancing activity at low concentrations – weak binding to virion – domain non-immunogenic in humans [Niedrig1992a]				
702	polyclonal	gp160 (733–736)	gp41 (735–752 IIIB)	IEEE	L	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* Cowpea mosaic virus *HIV component:* gp41 peptide **Ab type** C-term **References** Cleveland2000b, McLain2001 • When PRGPDRPEGIEEEGGERDRDRS was used as antigen an immunodominant, non-neutralizing response to IEEE was observed, but immunization GERDRDR shifts the response to ERDRD [Cleveland2000b] • The substitution 725 RG (P[R–>G]GPDRPEGIEEEGGERDRDRS) alters the antigenic exposure of this region on the virion resulting in the loss of the downstream neutralizing epitope ERDRD, increased exposure of the epitope GPDRPEG in the virion, while the epitope IEEE remains unchanged [McLain2001]				
703	polyclonal	gp160 (733–736)	gp41 (735–752 NL43)	IEEE	L	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* Cowpea mosaic virus *HIV component:* gp41 peptide **Ab type** C-term **References** McLain2001 • The substitution 725 RG (P[R–>G]GPDRPEGIEEEGGERDRDRS) alters the antigenic exposure of this region on the virion resulting in the loss of the downstream neutralizing epitope ERDRD, increased exposure of the epitope GPDRPEG in the virion, while the epitope IEEE remains unchanged [McLain2001]				
704	B8	gp160 (733–741)	gp41 (733–741 BH10)	IEEEGGERD	no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *Strain:* LAI *HIV component:* gp160 **References** Pincus1993b, Abacioglu1994 • B8: Ab response in IIIB lab workers was compared to gp160 LAI vaccine recipients – B8 was used as a control – the dominant response among vaccinees was to this mid-gp41 region, but not among the infected lab workers – Abs binding this region do not neutralize, bind to infected cells, nor serve as immunotoxins [Pincus1993b] • B8: Epitope boundaries mapped by peptide scanning [Abacioglu1994]				
705	1577	gp160 (739–743)	gp41 (735–752 IIIB)	ERDRD	no	Vaccine	murine
		Vaccine *Vector/Type:* poliovirus *Strain:* IIIB *HIV component:* gp41 peptide **Ab type** C-term **Donor** C. Vella or Morag Ferguson (NIBSC, Potters Bar UK) **References** Evans1989, D'Souza1991, Vella1993, Cleveland2000a • 1577: Raised against IIIB peptide chimera – neutralized African and American HIV-1 lab strains [Evans1989] • 1577: Non-neutralizing in this multi-lab study [D'Souza1991]				

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 1577: Core epitope: ERDRD – could neutralize HIV IIIB and HIV RF [Vella1993] • 1577: Ab binding to IEEE suppresses neutralizing Ab binding to adjacent epitope ERDRD [Cleveland2000a] • 1577: UK Medical Research Council AIDS reagent: ARP317 • 1577: NIH AIDS Research and Reference Reagent Program: 1172					
706	polyclonal	gp160 (739–743)	gp41 (735–752 IIIB)	ERDRD	L	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* Cowpea mosaic virus *HIV component:* gp41 peptide **Ab type** C-term **References** Cleveland2000b, McLain2001 • ERDRD-specific IgG recognizes an externalized loop of the gp41 C-terminal tail with high affinity – neutralized HIV-1 B clade strains IIIB, NL-4.3, RF, MN and D clade virus CBL-4, but HXB-2D (clade B) was not recognized – when PRGPDRPEGIEEEGGERDRDRS was used as antigen an immunodominant, non-neutralizing response to IEEE was observed, but immunization GERDRDR shifts the response to ERDRD – NAb does not inhibit attachment of free virus, but does inhibit by an event that precedes fusion-entry [Cleveland2000b] • The substitution 725 RG (P[R–>G]GPDRPEGIEEEGGERDRDRS) alters the antigenic exposure of this region on the virion resulting in the loss of the downstream neutralizing epitope ERDRD, increased exposure of the epitope GPDRPEG in the virion, while the epitope IEEE remains unchanged [McLain2001]					
707	DZ	gp160 (822–855)	gp41 (827–860 BRU)	VAEGTDRVIEVVQGACRAIRHIPRR-IRQGLERIL	L	Vaccine	human (IgG1λ)
		Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* gp60 **References** Boyer1991 • DZ: Weakly neutralizing IIIB – binds to peptides 827-843 and 846-860 of BRU – reacted specifically with IIIB and RF [Boyer1991]					

IV-C-14 Env Antibodies

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
708		Env	gp120 (IIIB)			Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* gp120 *Adjuvant:* GM-CSF **References** Rodríguez1999 • The murine Ab response to a chimeric of granulocyte-macrophage colony stimulating factor GM-CSF/gp120 in vaccinia was not higher titer that the response to a gp120-vaccinia construct, but the breadth of the Ab response was greater, in particular to the C-term region of gp120 – a cellular response of greater intensity was trigged to the GM-CSF/gp120 vaccinia construct, as measured by Elispot assay [Rodríguez1999]				
709		Env	Env (384–467)			Vaccine	rabbit, Rhesus macaque
		Vaccine *Vector/Type:* hepatitis B surface antigen lipoprotein particles HsBAg *HIV component:* V3 *Adjuvant:* LAI **References** Michel1993 • Immunization with recombinant HIV1 V3/HBsAg hybrid particles into rabbits or macaques elicited and maintained for several months anti-V3 or HIV-1 Env proliferative, CTL and Ab responses [Michel1993]				
710		Env	gp120 and p55			Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* virus-like particle *Strain:* gp120 A clade UG5.94UG018, HIV-1 IIIB *HIV component:* gp120 and Pr55gag **References** Buonaguro2002 • BALB/c mice were given intraperitoneal immunization with virus-like particlea (VLPs) expressing recombinant subtype A gp120 and Pr55gag in the absence of adjuvants. High dose-independent humoral responses against both gp120 and p24 peptides were detected. Antibodies able to elicit 50% neutralization against IIIB and the autologous clade A virus were obtained [Buonaguro2002]				
711		Env			Y	HIV-1 infection, Vaccine	human
		References Burton2000 • This review article touches on why natural immune responses do not tend to favor potent neutralizing Ab production, and discusses possible vaccine strategies to counter this problem [Burton2000]					
712		Env			P	HIV-1 infection	human
		References Pellegrin1996 • Detection of an autologous NAb response in 12 patients with primary infections was delayed – for patients with a viral isolate obtained at month 1, autologous NAbs to viral isolates were generally not observed before month 6, and there was no apparent relationship between the emergence of neutralizing activity and the decrease of plasma viral load [Pellegrin1996]					
713	102-135	Env	gp41 (HAM112, O group)			Vaccine	murine (IgG1 κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* HAM112 (group O) *HIV component:* gp160 **References** Scheffel1999 • 102-135: Overlapping peptides based on group O HAM112 Env were tested for MAb reactivity – 102-135 bound to two non-contiguous peptides in combination, assumed to form some type of helical structure, and not to either individually [Scheffel1999]					
714	1025	Env	gp120				
		References Berman1997 • 1025: Binds to 1/7 isolates from breakthrough cases from a MN gp120 vaccine trial [Berman1997]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
715	105-134	Env	gp41 (652–681 HAM112, O group)			Vaccine	murine (IgG1 κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* HAM112 (group O) *HIV component:* gp160					
		References Scheffel1999					
		• 105-134: Overlapping peptides based on group O HAM112 Env were tested for MAb reactivity [Scheffel1999]					
716	10E9	Env	gp41			HIV-1 infection	murine (IgG1)
		References Papsidero1988					
		• 10E9: 100/100 HIV+ human sera could inhibit 10E9 binding [Papsidero1988]					
717	126-50	Env	gp41 (HXB2)		no	HIV-1 infection	human (IgG2κ)
		References Robinson1990b, Tyler1990, Robinson1991, Xu1991					
		• 126-50: No enhancing activity for HIV-1 IIIB [Robinson1990b]					
		• 126-50: Serves as target for antibody-dependent cellular cytotoxicity ADCC [Tyler1990]					
		• 126-50: No enhancing or neutralizing activity [Robinson1991]					
		• 126-50: Specific for a conformational epitope [Xu1991]					
718	12H2	Env	gp41 (530–677 HXB2)		no	Vaccine	murine (IgMκ)
		Vaccine *Vector/Type:* Semliki-Forest Virus *HIV component:* Env					
		References Giraud1999					
		• 12H2: Env in a Semliki-Forest Virus (SFV) vector was used to vaccinate mice intramuscularly as naked RNA, and an Ab response was induced to Env from which 12H2 was derived – and advantage of this method is that the protein is properly expressed [Giraud1999]					
719	13.10 (No. 13)	Env	gp120		no	HIV-1 infection	human (IgG1λ)
		Donor Evan Hersh and Yoh-Ichi Matsumoto					
		References Lake1989, Moran1993, Wisnewski1996					
		• 13.10: First HIV-1 specific human-mouse hybridoma that produces a MAb that binds to gp120 and gp160 [Lake1989]					
		• 13.10: Heavy (V HI) and light (V lambdaII) chain sequenced – no enhancing or neutralizing activity – called No. 13 [Moran1993]					
		• 13.10: 13.10 is V H1 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals [Wisnewski1996]					
		• 13.10: NIH AIDS Research and Reference Reagent Program: 377					
720	1B1	Env	Env		L	HIV-1 infection	human
		Donor Herman Katinger, Inst. Appl. Microbiol. University of Agricultural Science, Vienna, Austria					
		References Buchacher1994, Purtscher1994, Kunert1998					
		• 1B1: Generated by electrofusion of PBL from HIV-1 positive volunteers with CB-F7 cells [Buchacher1994]					
		• 1B1: The complete V, J and D(H) domain was sequenced – unlike non-neutralizing anti-gp41 MAb 3D6, five neutralizing MAbs (2F5, 2G12, 1B1, 1F7, and 3D5) showed extensive somatic mutations giving evidence of persistent antigenic pressure over long periods [Kunert1998]					
721	1F7	Env	Env		L	HIV-1 infection	human
		Donor Herman Katinger, Inst. Appl. Microbiol. University of Agricultural Science, Vienna, Austria					
		References Buchacher1994, Purtscher1994, Kunert1998, Grant2000					
		• 1F7: Generated by electrofusion of PBL from HIV-1 positive volunteers with CB-F7 cells [Buchacher1994]					
		• 1F7: The complete V, J and D(H) domain was sequenced – unlike non-neutralizing anti-gp41 MAb 3D6, five neutralizing MAbs (2F5, 2G12, 1B1, 1F7, and 3D5) showed extensive somatic mutations giving evidence of persistent antigenic pressure over long periods [Kunert1998]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 1F7: There is an anti-idiotype MAb named 1F7 that was raised against pooled IgG from HIV-1+ subjects that recognizes a set of antibodies against HIV Gag, Pol, and Env, and this MAb is reported to inhibit anti-HIV CTL activity—this is not the same as the 1F7 described by Buchacher *et al.* [Grant2000].					
722	2.2B	Env	gp41		no		
		References Binley1999, Schulke2002					
		• 2.2B: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes [Binley1999]					
		• 2.2B: Ab binding characteristics of SOS gp140 were tested using SPR and RIPA – SOS gp140 is gp120-gp41 bound by a disulfide bond – NAbs 2G12, 2F5, IgG1b12, CD4 inducible 17b, and 19b bound to SOS gp140 better than uncleaved gp140 (gp140unc) and gp120 – non-neutralizing MAbs 2.2B (binds to gp41 in gp140unc) and 23A (binds gp120) did not bind SOS gp140 [Schulke2002]					
723	30D	Env	gp120		no		
		References Yang2002					
		• 30D: Uncleaved soluble gp140 (YU2 strain, R5 primary isolate) can be stabilized in an oligomer by fusion with a C-term trimeric GCN4 motif or using a T4 trimeric motif derived from T4 bacteriophage fibritin—stabilized oligomer gp140Δ683(-FT) showed strong preferential recognition by NAbs IgG1b12 and 2G12 relative to the gp120 monomer, in contrast to poorly neutralizing MAbs F105, F91, 17b, 48d, and 39F which showed reduced levels of binding, and C11, A32, and 30D which did not bind the stabilized oligomer [Yang2002].					
724	31710B	Env	gp41				human (IgG1)
		References Alsmadi1998					
		• 31710B: A study of 6 anti-Env MAbs and their ability to bind or direct ADCC against target cells infected with IIIB, MN, SF-2, and RF – bound and directed lysis against all four strains [Alsmadi1998]					
725	38B5/C9	Env	gp120 (SF162)		no	Vaccine	human from transgenic mice (IgG2κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM)					
		Donor Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org					
		References He2002					
		• 38B5/C9: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—11 of the MAbs were conformation dependent, but did not block sCD4 binding—these MAbs were part of the same competition group, and enhanced binding of the CD4BS MAb 38G3/A9 and anti-CD4BS MAbs also enhanced their binding—these MAbs tended to be very cross-reactive but could not neutralize autologous SF162—38B5/C9 bound to most R5 and X4 B clade viruses, as well as one of two E clade viruses [He2002].					
726	39H10/A11	Env	gp120 (SF162)		no	Vaccine	human from transgenic mice (IgG2κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM)					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		Donor Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** He2002 • 39H10/A11: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—11 of the MAbs were conformation dependent, but did not block sCD4 binding—these MAbs were part of the same competition group, and enhanced binding of the CD4BS MAb 38G3/A9 and anti-CD4BS MAbs also enhanced their binding—these MAbs tended to be very cross-reactive but could not neutralize autologous SF162—39H10/A11 bound to three R5 and three X4 B clade viruses, as well as two E clade viruses [He2002].				
727	3D5	Env	Env		L	HIV-1 infection	human
		Donor Herman Katinger, Inst. Appl. Microbiol. University of Agricultural Science, Vienna, Austria **References** Buchacher1994, Purtscher1994, Kunert1998 • 3D5: Generated by electrofusion of PBL from HIV-1 positive volunteers with CB-F7 cells [Buchacher1994] • 3D5: The complete V, J and D(H) domain was sequenced – unlike non-neutralizing anti-gp41 MAb 3D6, five neutralizing MAbs (2F5, 2G12, 1B1, 1F7, and 3D5) showed extensive somatic mutations giving evidence of persistent antigenic pressure over long periods [Kunert1998]				
728	3H6	Env	gp41				murine
		References Pinter1995 • 3H6: There is another MAb with this ID that recognizes Rev [Orsini1995] • 3H6: Generated in response to virus grown in protein-free medium [Pinter1995]					
729	40D3/C11	Env	gp120 (SF162)		no	Vaccine	human from transgenic mice (IgG2κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) **Donor** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** He2002 • 40D3/C11: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—11 of the MAbs were conformation dependent, but did not block sCD4 binding—these MAbs were part of the same competition group, and enhanced binding of the CD4BS MAb 38G3/A9 and anti-CD4BS MAbs also enhanced their binding—these MAbs tended to be very cross-reactive but could not neutralize autologous SF162—40D3/C11 bound to most R5 and X4 B clade viruses, as well as one of two E clade viruses [He2002].				
730	49B11/A1	Env	gp120 (SF162)		no	Vaccine	human from transgenic mice (IgG2κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) **Donor** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** He2002 • 49B11/A1: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—11 of the MAbs were conformation dependent, but did not block sCD4 binding—these MAbs were part of the same competition group, and enhanced binding of the CD4BS MAb 38G3/A9 and anti-CD4BS MAbs also enhanced their binding—these MAbs tended to be very cross-reactive but could not neutralize autologous SF162—49B11/A1 bound to most R5 and X4 B clade viruses, as well as one of two E clade viruses [He2002].				

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
731	52G5/B9	Env	gp120 (SF162)		no	Vaccine	human from transgenic mice (IgG2κ)

Vaccine *Vector/Type:* recombinant protein *Strain:* SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM)
Donor Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References He2002

- 52G5/B9: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—11 of the MAbs were conformation dependent, but did not block sCD4 binding—these MAbs were part of the same competition group, and enhanced binding of the CD4BS MAb 38G3/A9 and anti-CD4BS MAbs also enhanced their binding—these MAbs tended to be very cross-reactive but could not neutralize autologous SF162—52G5/B9 bound to most R5 and X4 B clade viruses, as well as one of two E clade viruses [He2002].

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
732	55E4/H1	Env	gp120 (SF162)		no	Vaccine	human from transgenic mice (IgG2κ)

Vaccine *Vector/Type:* recombinant protein *Strain:* SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM)
Donor Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References He2002

- 55E4/H1: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—11 of the MAbs were conformation dependent, but did not block sCD4 binding—these MAbs were part of the same competition group, and enhanced binding of the CD4BS MAb 38G3/A9 and anti-CD4BS MAbs also enhanced their binding—these MAbs tended to be very cross-reactive but could not neutralize autologous SF162—55E4/H1 bound to most R5 and X4 B clade viruses, as well as one of two E clade viruses [He2002].

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
733	56C4/C8	Env	gp120 (SF162)		no	Vaccine	human from transgenic mice (IgG2κ)

Vaccine *Vector/Type:* recombinant protein *Strain:* SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM)
Donor Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References He2002

- 56C4/C8: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—11 of the MAbs were conformation dependent, but did not block sCD4 binding—these MAbs were part of the same competition group, and enhanced binding of the CD4BS MAb 38G3/A9 and anti-CD4BS MAbs also enhanced their binding—these MAbs tended to be very cross-reactive but could not neutralize autologous SF162—56C4/C8 bound to some R5 and X4 B clade viruses, as well as one of two E clade viruses [He2002].

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
734	57B6/F1	Env	gp120 (SF162)		no	Vaccine	human from transgenic mice (IgG2κ)

Vaccine *Vector/Type:* recombinant protein *Strain:* SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM)
Donor Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References He2002

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 57B6/F1: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—11 of the MAbs were conformation dependent, but did not block sCD4 binding—these MAbs were part of the same competition group, and enhanced binding of the CD4BS MAb 38G3/A9 and anti-CD4BS MAbs also enhanced their binding—these MAbs tended to be very cross-reactive but could not neutralize autologous SF162—57B6/F1 bound some R5 and X4 B clade viruses, and no E clade viruses [He2002].					
735	57H5/D7	Env	gp120 (SF162)		no	Vaccine	human from transgenic mice (IgG2κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) **Donor** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** He2002 • 57H5/D7: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—11 of the MAbs were conformation dependent, but did not block sCD4 binding—these MAbs were part of the same competition group, and enhanced binding of the CD4BS MAb 38G3/A9 and anti-CD4BS MAbs also enhanced their binding—these MAbs tended to be very cross-reactive but could not neutralize autologous SF162—57H5/D7 bound to most R5 and X4 B clade viruses, as well as one of two E clade viruses [He2002].					
736	63G4/E2	Env	gp120 (SF162)		no	Vaccine	human from transgenic mice (IgG2κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) **Donor** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** He2002 • 63G4/E2: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—11 of the MAbs were conformation dependent, but did not block sCD4 binding—these MAbs were part of the same competition group, and enhanced binding of the CD4BS MAb 38G3/A9 and anti-CD4BS MAbs also enhanced their binding—these MAbs tended to be very cross-reactive but could not neutralize autologous SF162—63G4/E2 bound to three R5 and three X4 B clade viruses, as well as two E clade viruses [He2002].					
737	65B12/C5	Env	gp120 (SF162)		no	Vaccine	human from transgenic mice (IgG2κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) **Donor** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** He2002 • 65B12/C5: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—11 of the MAbs were conformation dependent, but did not block sCD4 binding—these MAbs were part of the same competition group, and enhanced binding of the CD4BS MAb 38G3/A9 and anti-CD4BS MAbs also enhanced their binding—these MAbs tended to be very cross-reactive but could not neutralize autologous SF162—65B12/C5 bound some R5 and X4 B clade viruses, and no E clade viruses [He2002].					
738	6E10	Env	gp120		L	Vaccine	
		Vaccine *Vector/Type:* recombinant protein *HIV component:* gp160					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		Donor Phil Berman **References** Berman1991					
739	7-1054	Env	gp36 (HIV-2)		no		murine
		References Scheffel1999 • Binds HIV-2 gp36, used as a control in a study of group O MAbs [Scheffel1999]					
740	7B2	Env	gp41		no		
		References Binley1999 • 7B2: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes [Binley1999]				
741	85G11/D8	Env	gp120 (SF162)		no	Vaccine	human from transgenic mice (IgG2κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* SF162 *HIV component:* deglycosylated gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) **Donor** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** He2002 • 85G11/D8: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—three of the MAbs were conformation dependent, but did not block sCD4 binding and were part of the same competition group—these MAbs were all raised against a deglycosylated form of gp120—they could not neutralize autologous SF162 and bound some R5 and X4 B clade viruses, and no E clade viruses [He2002].					
742	87E4/A8	Env	gp120 (SF162)		no	Vaccine	human from transgenic mice (IgG2κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* SF162 *HIV component:* deglycosylated gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) **Donor** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** He2002 • 87E4/A8: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—three of the MAbs were conformation dependent, but did not block sCD4 binding and were part of the same competition group—these MAbs were all raised against a deglycosylated form of gp120—they could not neutralize autologous SF162 and bound some R5 and X4 B clade viruses, and no E clade viruses [He2002].					
743	97B1/E8	Env	gp120 (SF162)		no	Vaccine	human from transgenic mice (IgG2κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* SF162 *HIV component:* deglycosylated gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) **Donor** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References He2002					
		• 97B1/E8: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—three of the MAbs were conformation dependent, but did not block sCD4 binding and were part of the same competition group—these MAbs were all raised against a deglycosylated form of gp120—they could not neutralize autologous SF162 and bound some R5 and X4 B clade viruses, and no E clade viruses [He2002].					
744	A9	Env	gp120 (IIIB)			Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* chimeric GM-CSF *Strain:* IIIB *HIV component:* gp120 *Adjuvant:* GM-CSF					
		References delReal1999					
		• A9: Murine antibody response to the chimeric construction granulocyte-macrophage colony stimulating factor GM-CSF/gp120 was tested, MAbs from normal mice were gp120 specific, MAbs from nude mice bound gp120 but were polyreactive, and from reconstituted mice were half way between – the anti-gp120 response used a high frequency of VH81X, VHQ52, and VH7183 genes, a family used during fetal life and associated with autoimmunity – A9 was a gp120 from a BALBc reconstructed nude mouse and had VH gene 7183-2 [delReal1999]					
745	B4	Env	gp120 (IIIB)			Vaccine	murine (IgM)
		Vaccine *Vector/Type:* chimeric GM-CSF *Strain:* IIIB *HIV component:* gp120					
		References delReal1999					
		• B4: Murine antibody response to the chimeric construction granulocyte-macrophage colony stimulating factor GM-CSF/gp120 was tested, MAbs from normal mice were gp120 specific, MAbs from nude mice bound gp120 but were polyreactive, and from reconstituted mice were half way between – the anti-gp120 response used a high frequency of VH81X, VHQ52, and VH7183 genes, a family used during fetal life and associated with autoimmunity – B4 was an anti-gp120 from a BALBc reconstructed nude mouse and had VH gene J606 [delReal1999]					
746	B5	Env	gp120 (IIIB)			Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* chimeric GM-CSF *Strain:* IIIB *HIV component:* gp120 *Adjuvant:* GM-CSF					
		References delReal1999					
		• B5: Murine antibody response to the chimeric construction granulocyte-macrophage colony stimulating factor GM-CSF/gp120 was tested, MAbs from normal mice were gp120 specific, MAbs from nude mice bound gp120 but were polyreactive, and from reconstituted mice were half way between – the anti-gp120 response used a high frequency of VH81X, VHQ52, and VH7183 genes, a family used during fetal life and associated with autoimmunity – B5 was a gp120 specific MAb from a BALBc mouse and had VH gene J558 [delReal1999]					
747	B6	Env	gp120 (IIIB)			Vaccine	murine (IgM)
		Vaccine *Vector/Type:* chimeric GM-CSF *Strain:* IIIB *HIV component:* gp120					
		References delReal1999					
		• B6: Murine antibody response to the chimeric construction granulocyte-macrophage colony stimulating factor GM-CSF/gp120 was tested, MAbs from normal mice were gp120 specific, MAbs from nude mice bound gp120 but were polyreactive, and from reconstituted mice were half way between – the anti-gp120 response used a high frequency of VH81X, VHQ52, and VH7183 genes, a family used during fetal life and associated with autoimmunity – B6 was a gp120 from a BALBc reconstructed nude mouse and had VH gene J558 [delReal1999]					
748	BAT267	Env	gp120		L	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* inactivated virus *Strain:* IIIB *HIV component:* virus					
		References Fung1987					
749	BAT401	Env	gp120		L	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* inactivated virus *Strain:* IIIB *HIV component:* virus					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Fung1987					
750	BAT509	Env	gp120		L	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* inactivated virus *Strain:* IIIB *HIV component:* virus **References** Fung1987					
751	C31	Env	gp120		no	HIV-1 infection	human (IgG1κ)
		References Boyer1991 • C31: Broadly-reactive group specific MAb – high yield cultivation of human MAb [Boyer1991]					
752	D1	Env	gp41 (IIIB)			Vaccine	murine (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140 **References** Otteken1996 • D1: MAbs D1, D16, had T37 bind to oligomeric gp160 equally well – pulse label experiments of MAb binding to noncleavable gp160 revealed that these MAbs bound with a delay, epitopes forming with a half life of 30 min [Otteken1996]					
753	D12	Env	gp41 (IIIB)		L	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140 **Donor** Patricia Earl and Christopher Broder, NIH **References** Earl1994, Broder1994, Richardson1996, Earl1997, Otteken1996, LaBranche1999 • D12: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response [Earl1994] • D12: One of 18 MAbs (e. g. D4 and D40) that bind to a conformation-dependent epitope in gp41 that bind preferentially, but not exclusively, to oligomers – neutralizes IIIB and SF2 [Broder1994] • D12: This antibody was blocked more strongly by human sera than other anti-gp41 MAbs (D20, D43, D61, and T4) in a oligomeric ELISA assay [Richardson1996] • D12: MAbs D10 and D12 are very easily blocked by human sera from HIV+ individuals [Earl1997] • D12: MAbs D4, D10, D11, D12, and D41 all bind only to complete oligomer – pulse label experiments of MAb binding to noncleavable gp160 revealed that these MAbs bound with a delay, epitopes forming with a half life of 30 min [Otteken1996] • D12: D12 was used in WB of HIV-1 transmembrane proteins in a study which showed that determinants of HIV-1 CD4 independence map outside regions required for coreceptor specificity – IIIBx, a CD4-independent variant of IIIB, has a truncated gp41 [LaBranche1999] • D12: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) – gp41 MAbs T4, D12, T3, and D50 bound less efficiently to gp140-GNC4 than did pooled sera, but T4 and D12 recognized the gp140-GNC4 timer equivalently to gp140(-), and T3 and D50 recognized the trimer at greater levels than gp140(-) [Yang2000]					
754	D16	Env	gp41 (IIIB)		L	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* dimeric Env **Donor** Patricia Earl and Christopher Broder, NIH **References** Earl1994, Weissenhorn1996, Earl1997 • D16: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response [Earl1994] • D16: Precipitates both oligomeric gp140 and soluble monomeric gp41(21-166)that lacks the fusion peptide and membrane anchor, along with MAbs D16, D38, D40, D41, and D54 [Weissenhorn1996] • D16: One of eleven MAbs (D16, D17, D31, D36, D37, D40, D44, D55, D59, T37, and T45) that are conformation dependent and that can block the binding of the MAb D50 that binds to the linear peptide gp41(642-665) – reactive with 9/10 HIV-1 strains all except HIV-1 ADA, which has the change E659D and E662A that may result in the loss of binding (ELLE to DLLA) [Earl1997]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
755	D4	Env	gp120 (IIIB)			Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* chimeric GM-CSF *Strain:* IIIB *HIV component:* gp120					
		References delReal1999					
		• D4: Murine antibody response to the chimeric construction granulocyte-macrophage colony stimulating factor GM-CSF/gp120 was tested, MAbs from normal mice were gp120 specific, MAbs from nude mice bound gp120 but were polyreactive, and from reconstituted mice were half way between – the anti-gp120 response used a high frequency of VH81X, VHQ52, and VH7183 genes, a family used during fetal life and associated with autoimmunity – D4 was a gp120 from a BALBc reconstructed nude mouse and had VH gene J558 [delReal1999]					
756	D43	Env	gp41 (HXB2)			Vaccine	murine (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* dimeric Env					
		Donor Patricia Earl and Christopher Broder, NIH					
		References Earl1994, Richardson1996, Earl1997					
		• D43: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response [Earl1994]					
		• D43: This is a linear gp41 epitope, mapping in the region 635-678 – human sera blocked binding in oligomeric ELISA assay to a similar extent for gp41 MAbs D20, D43, D61, and T4 [Richardson1996]					
		• D43: Partially conformation dependent – doesn't bind to short peptides, but does bind to the region spanning 641-683 – binding can be blocked by MAbs T3, D38 and D45 – MAbs in this competition group reacted with 9/10 HIV-1 strains, not binding to JRFL [Earl1997]					
757	F223	Env	gp120		no	HIV-1 infection	human (IgG3λ)
		References Cavacini1999					
		• F223: binds to HIV-1 gp120 and to uninfected lymphocytes binding to a 159-kd auto-antigen expressed on most B cells and a small fraction of T and NK cells – the antibody enhances HIV-1 infection in a complement-dependent manner – F223 light chains have a strong homology with VLgamma2, the heavy chain to the germline gene VH3-H.11 – N-linked carbohydrates are key for recognition of both gp120 and the autoantigen – MAb 3D6 also uses VH3 and has autoreactivity [Cavacini1999]					
758	F285	Env	Env			HIV-1 infection	human (IgG1)
		References Wisnewski1995, Wisnewski1996					
		• F285: F285 is V H1 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals [Wisnewski1996]					
759	F7	Env	gp120 (IIIB)			Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* chimeric GM-CSF *Strain:* IIIB *HIV component:* gp120 *Adjuvant:* GM-CSF					
		References delReal1999					
		• F7: Murine antibody response to the chimeric construction granulocyte-macrophage colony stimulating factor GM-CSF/gp120 was tested, MAbs from normal mice were gp120 specific, MAbs from nude mice bound gp120 but were polyreactive, and from reconstituted mice were half way between – the anti-gp120 response used a high frequency of VH81X, VHQ52, and VH7183 genes, a family used during fetal life and associated with autoimmunity – F7 was a gp120 specific MAb from a BALBc mouse and had VH gene 7183(81X), previously found expressed only in fetal liver [delReal1999]					
760	Fab A12	Env	gp41 (LAI)		no	HIV-1 infection	human (IgG1κ)
		References Binley1996					
		• Fab A12: Uncharacterized epitope – variable regions sequenced [Binley1996]					
761	Fab A2	Env	gp41 (LAI)		no	HIV-1 infection	human (IgG1λ)
		References Binley1996					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• Fab A2: Uncharacterized epitope – variable regions sequenced [Binley1996]					
762	Fab L9	Env	gp41 (LAI)		no	HIV-1 infection	human (IgG1κ)
		References Binley1996					
		• Fab L9: Uncharacterized epitope – variable regions sequenced [Binley1996]					
763	G12	Env	gp120 (IIIB)			Vaccine	murine (IgM)
		Vaccine *Vector/Type:* chimeric GM-CSF *Strain:* IIIB *HIV component:* gp120					
		References delReal1999					
		• G12: Murine antibody response to the chimeric construction granulocyte-macrophage colony stimulating factor GM-CSF/gp120 was tested, MAbs from normal mice were gp120 specific, MAbs from nude mice bound gp120 but were polyreactive, and from reconstituted mice were half way between – the anti-gp120 response used a high frequency of VH81X, VHQ52, and VH7183 genes, a family used during fetal life and associated with autoimmunity – G12 was a gp120 from a BALBc reconstructed nude mouse and had VH gene 7183-6 [delReal1999]					
764	G2	Env	gp120 (IIIB)			Vaccine	murine (IgM)
		Vaccine *Vector/Type:* chimeric GM-CSF *Strain:* IIIB *HIV component:* gp120					
		References delReal1999					
		• G2: Murine antibody response to the chimeric construction granulocyte-macrophage colony stimulating factor GM-CSF/gp120 was tested, MAbs from normal mice were gp120 specific, MAbs from nude mice bound gp120 but were polyreactive, and from reconstituted mice were half way between – the anti-gp120 response used a high frequency of VH81X, VHQ52, and VH7183 genes, a family used during fetal life and associated with autoimmunity – G2 was a gp120 from a BALBc reconstructed nude mouse and had VH gene Q52 [delReal1999]					
765	H2	Env	gp41				human (IgMκ)
		Donor BioInvent, Lund, Sweden, commercial					
		References Muller1991					
		• H2: Anti-idiotypic MAbs (10B3 and 2All) against MAb H2 were generated by immunization of BALBc mice with H2 – they also react with seropositive sera [Muller1991]					
766	H8	Env	gp120 (IIIB)			Vaccine	murine (IgM)
		Vaccine *Vector/Type:* chimeric GM-CSF *Strain:* IIIB *HIV component:* gp120					
		References delReal1999					
		• H8: Murine antibody response to the chimeric construction granulocyte-macrophage colony stimulating factor GM-CSF/gp120 was tested, MAbs from normal mice were gp120 specific, MAbs from nude mice bound gp120 but were polyreactive, and from reconstituted mice were half way between – the anti-gp120 response used a high frequency of VH81X, VHQ52, and VH7183 genes, a family used during fetal life and associated with autoimmunity – H8 was a gp120 from a BALBc reconstructed nude mouse and had VH gene Q52 [delReal1999]					
767	HBW4	Env	gp120 (IIIB)			HIV-1 infection	human (IgG1λ)
		References Moran1993, Wisnewski1995, Wisnewski1996					
		• HBW4: Heavy (V HII) and light (V lambdaII) chain sequenced [Moran1993]					
		• HBW4: HBW4 is V H2 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals [Wisnewski1996]					
768	HIVIG	Env	gp120		P	HIV-1 infection	human
		References Nichols2002					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• NYBC-HIVIG derived from patients with high NAb titers and NABI-HIVIG derived from patients with high anti-p24 Ab titers were compared in neutralizing assay against a panel of six primary isolates – both could neutralize all isolates tested but the NYBC-HIVIG dose required for 50% neutralization was of 3.2 fold lower, showing source plasmas influence the effective concentration of NAb present in HIVIG [Nichols2002]					
769	IVI-4G6	Env	gp41			Vaccine	murine (IgG2b)
		Donor K. Miyakoshi (Feji-Rebio Co, Tokyo, Japan) **References** Yin2001 • IVI-4G6: A bi-specific Ab (BFA) was made by combining Fab fragments of gp41-specific MAb IVI-4G6 and CD3-specific Mab UCHT1 – the BFA suppressed HIV-1 propagation culture and eliminated latently infected cells [Yin2001]					
770	K14	Env	gp41		no		human (IgG1)
		References Teeuwsen1990, Schutten1995a, Schutten1995b, Schutten1996, Schutten1997 • K14: Did not bind to peptides spanning gp41, but it does not react with Env deletion mutant 643-692 – does not react with HIV-2 – competition experiments showed this was an immunodominant conserved epitope in HIV-1 positive sera from Europe and Africa [Teeuwsen1990] • K14: Reduced affinity for both SI and NSI viruses relative to MAb MN215, failed to neutralize SI strain [Schutten1995b] • K14: In a study of NSI and SI virus neutralization, K14 did not influence viral entry [Schutten1997]					
771	M25	Env	gp41			Vaccine	murine (IgGκ)
		Vaccine *Vector/Type:* purified HIV-1 **References** diMarzo Veronese1985, Watkins1996 • M25: heavy and light chains cloned and sequenced – binding requires heavy and light chain in combination, in contrast to M77 [Watkins1996]					
772	MAG 6B	Env	gp120		no	Vaccine	murine
		Vaccine *Vector/Type:* sCD4-gp120 complex *Strain:* HXB2 *HIV component:* gp120 **Donor** C. Y. Kang, IDEC Inc **References** Kang1994 • MAG 6B: Amino acid substitutions that reduce binding 10 fold: 256 S/Y, 257 T/R or G or A, 262 N/T, 368 D/R or T, 370 E/R or Q, 381 E/P, 384 Y/E, 421 K/L, 475 M/S, 477 D/V [Kang1994]					
773	MO28	Env	gp41		no	in vitro stimulation	human (IgM)
		References Ohlin1989 • MO28: This antibody was raised by in vitro stimulation with a recombinant Env penv9 – the discontinuous epitope involves hydrophobic regions 632-646, 677-681 and 687-691, proximal to and spanning the transmembrane region – this specificity is unusual in HIV-1 positive sera [Ohlin1989]					
774	MO30	Env	gp41		no	in vitro stimulation	human (IgM)
		References Ohlin1989 • MO30: This antibody was raised by in vitro stimulation with a recombinant Env penv9 – the discontinuous epitope involves hydrophobic regions 632-646, 677-681 and 687-691, proximal to and spanning the transmembrane region – this specificity is unusual in HIV-1 positive sera [Ohlin1989]					
775	MO43	Env	gp41		no	in vitro stimulation	human (IgM)
		References Ohlin1989 • MO43: This antibody was raised by in vitro stimulation with a recombinant Env penv9 – the discontinuous epitope of MO43 involves hydrophobic regions 632-646, 677-681 and 687-691, proximal to and spanning the transmembrane region – this specificity is unusual in HIV-1 positive sera [Ohlin1989]					
776	N2-4	Env	gp41		no	HIV-1 infection	human (IgG1κ)
		Donor Evan Hersh and Yoh-Ichi Matsumoto					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Robinson1990b • N2-4: No enhancing activity for HIV-1 IIIB [Robinson1990b] • N2-4: NIH AIDS Research and Reference Reagent Program: 528					
777	N70-2.3a	Env	gp120 (dis)		no	HIV-1 infection	human (IgG1)
		Donor James Robinson, Tulane University, LA **References** Robinson1990a, Takeda1992 • N70-2.3a: Broad reactivity [Robinson1990a] • N70-2.3a: Fc receptor mediated enhancement of HIV-1 infection – binds a conformational site in the carboxyl half of gp120, distinct from 1.5e [Takeda1992]					
778	P43110	Env	gp120				
		Donor Advanced Biosciences (Kensington, MD) **References** diMarzo Veronese1992, VanCott1995 • P43110: Does not recognized denatured form of the gp120 protein [VanCott1995]					
779	P5-3	Env	gp120			HIV-1 infection	human (IgG1λ)
		Donor Evan Hersh and Yoh-Ichi Matsumoto **References** Robinson1990b, Pincus1991 • P5-3: No enhancing activity for HIV-1 IIIB [Robinson1990b] • P5-3: Poor immunotoxin activity when coupled to RAC – isotype specified as: IgG3lambda [Pincus1991] • P5-3: NIH AIDS Research and Reference Reagent Program: 378					
780	T15G1	Env	gp41		no		
		References Binley1999 • T15G1: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes [Binley1999]					
781	T20	Env	gp120 (IIIB)		no	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140 **Donor** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD **References** Earl1994, Otteken1996, Sugiura1999 • T20: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response [Earl1994] • T20: Pulse label experiments of 4 MAbs (D20, D27, T20, and T22) binding to noncleavable gp140 revealed that these anti-CD4BS MAbs bound with a delay, and that the epitope formed with a t 1/2 of about 10 minutes [Otteken1996] • T20: A comparison of 25 gp120 specific, conformation dependent MAbs was done – T20 is part of a group of MAbs labeled AII – all AII MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, and could only partially blocked CD4 binding [Sugiura1999]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
782	T27	Env	gp120 (IIIB)		no	Vaccine	murine (IgG)

Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140
Donor P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References Earl1994, Sugiura1999

- T27: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response [Earl1994]
- T27: A comparison of 25 gp120 specific, conformation dependent MAbs was done – T27 is part of a group of MAbs labeled AII – all AII MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, and could only partially blocked CD4 binding [Sugiura1999]

783	T3	Env	gp41 (HXB2)			Vaccine	murine (IgG)

Vaccine *Vector/Type:* tetrameric Env *HIV component:* Env
References Earl1994, Earl1997, Zwick2001b, Yang2000

- T3: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response [Earl1994]
- T3: Partially conformation dependent – doesn't bind to short peptides, but does bind to the region spanning 641-683 – binding can be blocked by MAbs D43, D38 and D45 – MAbs in this competition group reacted with 9/10 HIV-1 strains, not binding to JRFL [Earl1997]
- T3: T3 partially competes with MAb Z13, but not MAb 4E10, both of which bind to gp41 proximally to the 2F5 epitope and have a broad neutralizing potential [Zwick2001b]
- T3: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) – gp41 MAbs T4, D12, T3, and D50 bound less efficiently to gp140-GNC4 than did pooled sera, but T4 and D12 recognized the gp140-GNC4 timer equivalently to gp140(-), and T3 and D50 recognized the trimer at greater levels than gp140(-) [Yang2000]

784	T30	Env	gp41		no	Vaccine	murine

Vaccine *Vector/Type:* tetrameric Env *HIV component:* Env
References Earl1994, Earl1997

- T30: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response [Earl1994]
- T30: Binds in the region 580 to 640, but does not bind to peptides spanning this region – binding depends on N-linked glycosylation of Asn 616 – no other antibody tested inhibited binding, but binding could be inhibited by sera from HIV+ individuals [Earl1997]

785	T4	Env	gp41 (IIIB)		L	Vaccine	murine (IgG)

Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140
References Earl1994, Broder1994, Richardson1996, Weissenhorn1996, Otteken1996, Earl1997, Binley1999, Stamatatos2000, Yang2000, Srivastava2002

- T4: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response [Earl1994]
- T4: one of five MAbs (T4, T6, T9, T10 and T35) in a competition group that bind to a conformation-dependent epitope in gp41 and is oligomer specific – neutralizes IIIB and SF2 [Broder1994]
- T4: Does not bind to soluble monomeric gp41(21-166) that lacks the fusion peptide and membrane anchor, only to the oligomer gp140, as does T6 [Weissenhorn1996]
- T4: MAbs T4 and T6 bind only to oligomer, and pulse chase experiments indicate that the epitope is very slow to form, requiring one to two hours [Otteken1996]
- T4: This antibody, along with 7 others (M10, D41, D54, T6, T9, T10 and T35), can block the linear murine MAb D61, and the human MAb 246-D, which both bind to the immunodominant region near the two Cys in gp41 – most of these antibodies are oligomer dependent – all of the MAbs are reactive with ten different HIV-1 strains – members of this competition group are blocked by sera from HIV-1+ individuals [Earl1997]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- T4: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes [Binley1999]
- T4: Soluble gp140 derived from SF162, a neutralization-resistant primary isolate, and SF162AV2 a neutralization-susceptible isolate with 30 amino acids deleted from the V2 loop, were generated with or without the gp120-gp41 cleavage site intact – all forms are recognized by oligomer-specific MAb T4 and show enhanced binding of CD4i MAb 17b when sCD4 is bound – the fused forms are less efficiently recognized than the cleaved forms by polyclonal neutralizing sera from HIV-infected patients – the V3 loop is more exposed on the fused form [Stamatatos2000]
- T4: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) – gp41 MAbs T4, D12, T3, and D50 bound less efficiently to gp140-GNC4 than did pooled sera, but T4 and D12 recognized the gp140-GNC4 timer equivalently to gp140(-), and T3 and D50 recognized the trimer at greater levels than gp140(-) [Yang2000]
- T4: Oligomeric gp140 (o-gp140) derived from R5 primary isolate US4 was characterized for use as a vaccine reagent – antigen capture ELISA was used to compare the antigenicity of gp120 and o-gp140 using a panel of well characterized MAbs – T4 recognized o-gp140 [Srivastava2002]

786	multiple Fabs	Env	gp120			HIV-1 infection	human

References Burton1991

- A panel of anti-gp120 Fabs was generated by antigen selection from a random combinatorial library prepared from bone marrow from an asymptomatic individual [Burton1991]

787	multiple MAbs	Env	gp120			Vaccine	murine

Vaccine *Vector/Type:* protein *HIV component:* gp120
References Denisova1996

- When gp120 was used as an immunogen, in contrast to gp120 bound to an anti-V3 MAb, few MAbs were generated and all bound better to the native than to the denatured protein – MAbs generated were: G1B12, G2F7, G9G8, G12F12, G1B8, G11F11, G9E8, G1B11, G1B6, G6F2, G2E7 [Denisova1996]

788	multiple MAbs	Env	gp120			Vaccine	murine

Vaccine *Vector/Type:* gp120-CD4 complex *HIV component:* gp120
References Denisova1996

- When gp120-CD4 was used as an immunogen, in contrast to gp120 bound to an anti-V3 MAb, few MAbs were generated and all bound better to the native than to the denatured protein – MAbs generated were: CG43, CG41, CG49, CG53, CG42, CG4, CG46, CG40, CG52, CG51, CG48, CG50, CG125, CG124, CG121 [Denisova1996]

789	multiple MAbs	Env	gp120			Vaccine	murine

Vaccine *Vector/Type:* protein-Ab complex *HIV component:* gp120 complexed with MAb M77
References Denisova1996

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• When anti-V3 MAb M77 was bound to gp120 and used as an immunogen, it stimulated many MAbs to linear epitopes, as well as an array of MAbs to discontinuous epitope – 10 of 36 MAbs were mapped to linear epitopes and are mentioned elsewhere in this database, the others are: GV5H1, GV4D5, GV4G10, GV1A8, GV10H5, GV8E11, GV2H4, GV6E6, GV1F7, GV1G9, GV4G5, GV6B12, GV1E8, GV2B7, GV1B11, GV6H5, GV6G2, GV6B5, GV1E10, GV5E3, GV5B9, GV5F4, GV6G4, GV1A12, GV5C11, GV6B6, GV3C10 [Denisova1996]				
790	polyclonal	Env	Env		L P	HIV-1 infection	human (IgG3)
		References Scharf2001					
		• IgG3: HIVIG was separated into immunoglobulin classes and IgG3 neutralization of HIV strains X4, R5 and X4R5 strains was superior to IgG1 and IgG2, and IgG3 was also a more potent inhibitor of viral fusion – the IgG3 advantage was lost when only Fabs were considered, indicating the IgG3 neutralization efficacy is enhanced due to a longer hinge region of the heavy chain in comparison to IgG1 and IgG2 [Scharf2001]					
791	polyclonal	Env	gp140 (IIIB)		L	Vaccine	rabbit (IgG)
		Vaccine *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* gp140, gp120 *Adjuvant:* MPL-SE adjuvant, QS21 adjuvant					
		References Earl2001					
		• Immunization of rabbits with oligomeric gp140 induced production of higher levels of cross-reactive neutralizing Abs than immunization with gp120 – immunization of Rhesus macaques with gp140 yielded strong NAb against IIIB, modest against other lab-adapted strains, and no NAb activity against primary isolates – most neutralizing activity could not be blocked by a V3 peptide – 3/4 vaccinated macaques showed no viral replication upon intravenous challenge with SHIV-HXB2 [Earl2001]					
792	polyclonal	Env	gp160 (IIIB)			HIV-1 infection, Vaccine	human
		Vaccine *Vector/Type:* recombinant protein *Strain:* NL43 *HIV component:* gp160 *Adjuvant:* alum					
		References Cox1999					
		• 60 asymptomatic HIV-1 infected patients were vaccinated with rec gp160 in alum, produced in a baculovirus expression vector in insect cells (VaxSyn), 64 received placebo, and all were followed in a 5 year longitudinal study – a mean of 78% of vaccinated and 82% of those receiving placebo had demonstrable ADCC at the different time intervals in the study, and the vaccine did not enhance ADCC production – patients with rapid and slow disease progression showed similar ADCC levels [Cox1999]					
793	polyclonal	Env	gp160 (89.6)		yes	Vaccine	Rhesus macaque
		Vaccine *Vector/Type:* modified vaccinia Ankara *Strain:* 89.6 *HIV component:* SIVmac239 Gag/Pol and HIV-1 89.6P Env *Adjuvant:* IL2/Ig					
		References Barouch2001b					
		• Four rhesus macaques were vaccinated with a modified vaccinia Ankara (MVA) vaccine that elicited strong CTL responses as well as antibody responses. The animals were infected when challenged with pathogenic SHIV-89.6P, but had potent CTL responses, secondary NAb responses upon challenge, partial preservation of CD4+ T-cell counts, lower viral loads, and no evidence of disease or mortality by day 168 after challenge—monkeys that got a sham vaccine had high viral load, progressed to disease, and 2/4 were dead by day 168 [Barouch2001b].					
794	polyclonal	Env	gp160		no	HIV-1 infection	human
		References Ahmad2001					
		• High CD4+ T-cell count and low viral load was correlated with high ADCC anti-HIV-1 Env Ab titers in a study of 46 HIV-1 infected individuals from all disease stages [Ahmad2001]					
795	polyclonal	Env	gp160		P	HIV-1 infection	human (IgG)
		References Beirnaert2001					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• Neutralizing antibodies are thought to inhibit HIV entry by blocking either binding or fusion – six broadly cross-neutralizing sera that can neutralize group M and O viruses inhibit the binding to PBMCs – the nine primary isolates tested in this study represented very diverse subtypes and recombinant forms, and different co-receptor usage [Beirnaert2001]					
796	polyclonal	Env	gp160		P	HIV-1 infection	human (IgG)
		References Beirnaert2000					
		• Sera from 66 HIV individuals from diverse geographic locations could neutralize primary isolates to different extents: broad cross-neutralizing isolates could neutralize 14 primary isolates from HIV-1 group M clades A-H and three O isolates, limited cross-neutralizing sera neutralized some isolates, and non-neutralizing sera—6/7 broadly neutralizing sera were from African women, despite only 14/66 study subjects being women—ability to neutralize three key isolates, MN lab (envB/gagB, X4 coreceptor), VI525 (envG/gagH, envA/gagA, R5X4) and CA9 (Group O, R5) was predictive of being able to neutralize an additional set of 14 primary isolates [Beirnaert2000].					
797	polyclonal	Env	gp120 (SF2)		L	Vaccine	murine, baboon
		Vaccine *Vector/Type:* recombinant protein *Strain:* SF2 *HIV component:* gp120 *Adjuvant:* PLG+MF-59 microparticles					
		References O'Hagan2000					
		• Microparticles were used as an adjuvant for entrapped HIV-1 gp120 and induced strong serum IgG responses in mice – polylactide co-glycolide polymer (PLG) microparticles in combination with MF-59 had the highest response [O'Hagan2000]					
798	polyclonal	Env	gp120 (SF2, US4)			Vaccine	murine, guinea pig, macaque
		Vaccine *Vector/Type:* DNA, recombinant protein *Strain:* SF2, US4 *HIV component:* gp120 *Adjuvant:* PLG microparticles, aluminum phosphate, MF-59					
		References O'Hagan2001					
		• DNA vaccines of codon-optimized Env and Gag genes driven by CMV promotors and absorbed on to PLG microparticles were more effective than naked DNA at eliciting strong Ab responses (more rapid, higher titer, more stable), comparable to gp120 in MF-59 [O'Hagan2001]					
799	polyclonal	Env	gp120		L	HIV-1 infection	chimpanzee (IgG)
		References Shibata1999, Moore1999					
		• polyclonal: Purified IgG from chimpanzee sera infected with several HIV-1 strains was used for passive administration to macaques which were subsequently challenged with the virulent SHIV bearing the HIV-1 env DH12 – in vitro neutralization correlated with protection in vivo [Shibata1999]					
		• polyclonal: Commentary discussing this finding noting the particularly high neutralization titer and limited breadth of the chimpanzee sera used in this study [Moore1999]					
800	polyclonal	Env	gp160 (MN)		L P	HIV-1 infection	human (IgA)
		References Moja2000					
		• 15 samples isolated from parotid saliva were selected for study as they had anti-Env IgA – IgA neutralizing activity was detected that was not directed at either EDELKWA or the V3 loop [Moja2000]					
801	polyclonal	Env	gp120		L	Vaccine	
		Vaccine *Vector/Type:* recombinant protein *Strain:* SF2, MN *HIV component:* gp120					
		References McElrath2000					
		• After 3 immunizations, 210/241 (87%) HIV-1 uninfected vaccinees in a phase II trial developed NAbs – of 140 patients receiving 4 vaccinations, 53% had persistent neutralizing antibodies to homologous virus, and 34% to heterologous virus, measured at day 728 after initial immunization – immunogens were well tolerated– but IVDUs had a decreased Ab response relative to lower risk groups [McElrath2000]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
802	polyclonal	Env	gp120			Vaccine	murine
		Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* gp120 *Adjuvant:* GM-CSF/gp120 chimera **References** Rodríguez1999 • The murine Ab response to a chimeric of granulocyte-macrophage colony stimulating factor GM-CSF/gp120 in vaccinia was not higher titer that the response to a gp120-vaccinia construct, but the breadth of the Ab response was greater – a cellular response of greater intensity was trigged to the GM-CSF/gp120 vaccinia construct, as measured by proliferation and Elispot [Rodríguez1999]					
803	polyclonal	Env	gp120 (YU2)			Vaccine	murine (IgG)
		Vaccine *Vector/Type:* stabilized Env trimer *Strain:* YU2, HXBc2 *HIV component:* Env **Donor** Joseph Sodroski, Harvard Medical School **References** Yang2001 • Soluble Env trimers were created that were designed to mimic functional Env oligomers – stabilized timers could induce neutralizing antibodies more effectively than gp120, and Abs to the YU2 trimer were cross-reactive within clade B and could neutralize several primary and TCLA reactive strains – the stabilized primers did not neutralize primary isolates outside the B clade, from clades C, D, and E – HXBc2 stabilized trimer antigen elicited strong neutralizing Abs against the homologous isolate HXBc2 TCLA strain, but not against primary isolates [Yang2001]					
804	polyclonal	Env	gp120 (MN)			Vaccine	human
		Vaccine *Vector/Type:* recombinant protein *Strain:* MN *HIV component:* gp120 *Adjuvant:* QS21, alum **References** Evans2001 • Vaccination with QS21 adjuvant and rsgp120 elicited stronger and more sustained neutralizing antibody responses and lymphocyte proliferation with lower doses of rsgp120 than alum formulations, suggesting QS21 may be a means to reduce the does of soluble protein [Evans2001]					
805	polyclonal	Env	gp120		yes	HIV-1 infection	human
		References Binley2000 • HAART inhibited the development of anti-gp120 Ab when initiated during primary infection and sometimes in patients treated within 2 years of HIV-1 infection – HAART during primary infection usually did not inhibit the development of weak NAb responses against autologous virus – 3/4 patients intermittently adherent developed high titers of autologous NAbs, largely coincident with brief viremic periods [Binley2000]					
806	polyclonal	Env	gp120 (SIV)		yes	HIV-1 infection	macaque
		References Reitter1998 • This study concerned an SIV mutated strain that lacked 4th, 5th and 6th sites for N-linked glycosylation – monkeys infected with the mutant viruses had increased neutralizing activity in their sera relative to monkeys infected with the parental strain [Reitter1998]					
807	polyclonal	Env	Env		yes	HIV-1 infection	human
		References Kim2001 • After HAART reduction of viral load to <400 for three visits over a 12 month interval, 2/11 patients were found to have increased anti-Env Ab binding titers, and neutralizing Abs titers increased against primary isolates US1, and CM237 – no NAB titer increase was seen to more readily neutralized isolate BZ167 – this suggests that in certain individuals the control of HIV-1 by HAART may augment immune control of HIV [Kim2001]					
808	polyclonal	Env	Env		yes	HIV-1 exposed seronegative	human (IgA)
		References Kaul2001b • Kaul et al. provide a concise summary of the findings concerning the presence of Mucosal IgA in highly exposed, uninfected subjects, arguing for a role in protection [Kaul2001b]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
809	polyclonal	Env	gp120		yes	Vaccine	human
	Vaccine *Vector/Type:* recombinant protein *Strain:* SF2 *HIV component:* gp120 *Adjuvant:* MF-59 **References** Nitayaphan2000 • A phase I/II trial was conducted in 52 seronegative Thais immunizing with rgp120 SF2 – the vaccine was safe and 39/40 developed NAb responses to the autologous SF2, while 22/40 were able to cross-neutralize the heterologous strain MN [Nitayaphan2000]						
810	polyclonal	Env	gp120 (SF2)		yes	Vaccine	macaque
	Vaccine *Vector/Type:* recombinant protein *Strain:* SF2 *HIV component:* gp120, p24 *Adjuvant:* ISCOM **References** Heeney1998a • The immune responses induced in Rhesus monkeys using two different immunization strategies was studied – one vaccine group was completely protected from challenge infection, the other vaccinees and controls became infected – protected animals had high titers of heterologous NAbs, and HIV-1-specific T helper responses – increases in RANTES, MIP 1 alpha and MIP 1 beta produced by circulating CD8+ T cells were also associated with protection [Heeney1998a]						
811	polyclonal	Env	gp120			Vaccine	macaque
	Vaccine *Vector/Type:* peptide, recombinant protein *Strain:* SF2, SF33 *HIV component:* gp120 *Adjuvant:* ISCOM, MF-59 **References** Verschoor1999 • Attempts were made to broaden immune responses induced in Rhesus monkeys by immunization of animals previously immunized that had resisted homologous challenge, with a second immunization with ISCOM-peptides or a boost with gp120 from SF33 – animals didn't survive a second challenge heterologous challenge virus SHIV(SF33) raising concerns about early antigenic sin [Verschoor1999]						
812	polyclonal	Env	gp120		yes	Vaccine	baboon
	Vaccine *Vector/Type:* recombinant protein *Strain:* SF2 (subtype B), CM235 (CRF01) *HIV component:* gp120 *Adjuvant:* MF-59 **References** VanCott1999 • Immunization with rgp120 CM235 (CRF01) induced Abs capable of neutralizing TCLA subtype E (CRF01) and subtype B isolates, while rgp120SF2 induced Abs could only neutralize subtype B TCLA isolates – neither immunogen induced Abs capable of neutralizing primary HIV-1 isolates – both rgp120CM235 and rgp120SF2 induced Abs to regions within C1, V1/V2, V3, and C5, but unique responses were induced by rgp120CM235 to epitopes within C2, and by rgp120SF2 to multiple epitopes within C3, V4, and C4 – CM235 baboon sera bound 3- to 12-fold more strongly than the SF2 baboon sera to all subtype E gp120s while binding to subtype B gp120s (except SF2) were within two to threefold for the SF2 and CM235 baboon sera [VanCott1999]						
813	polyclonal	Env	gp140 (SF162DeltaV2)		yes	Vaccine	rabbit, Rhesus macaque (IgG)
	Vaccine *Vector/Type:* DNA with CMV promotor *Strain:* SF162, SF162ΔV2 *HIV component:* gp140 *Adjuvant:* MF-59C **References** Barnett2001 • SF162ΔV2 is a virus that has a 30 amino acids deletion in the V2 loop that does not abrogate its infectivity but renders it highly susceptible to neutralization—when incorporated into a codon-optimized DNA vaccine with a CMV promoter and delivered by gene gun, SF162ΔV2 gave higher neutralizing Ab titers against SF162 than did SF162 itself, and Abs that cross-neutralized non-homologous primary isolates were obtained only when SF162ΔV2, but not intact SF162, was used as the immunogen—Control MAbs 2F5 and 2G12 could neutralize all of the following primary isolates: 91US056(R5), 92US714(R5), 92US660(R5), 92HT593(R5X4), and BZ167(R5X4), while after the first protein boost, the sera from two SF162ΔV2 immunized macaques could neutralize 91US056(R5), 92US714(R5), 92US660(R5) and ADA(R5), but not 92HT593(R5X4) or 92US657(R5)—the pattern of cross-recognition shifted after the second boost [Barnett2001].						
814	polyclonal	Env	gp120			HIV-1 infection	human (IgG)
	References Binley1997b						

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• Retention of anti-Env antibodies and loss of anti-Gag antibodies during progression was studied, and suggested to be the result of the loss of T-cell help and the unique ability of Env to stimulate B cells even in a backdrop of declining CD4 cells, because of the ability of Env to bind to the CD4 molecule [Binley1997b]					
815	polyclonal	Env	gp120 (W61D)		L	Vaccine	human
		Vaccine *Vector/Type:* recombinant protein *Strain:* W61D *HIV component:* gp120 **References** Beddows1999					
		• rgp120 derived from a R5X4 subtype B virus, HIV-1 W61D, was used to vaccinate healthy volunteers and the resulting sera were compared with HIV-1 positive subjects – vaccinee sera had more potent responses to linear V1/V2 and V3 epitopes than did the sera from HIV-1+ individuals, but could only neutralize homologous or heterologous virus only after adaptation to T-cell lines – neutralization activity was lost after re-adaptation to growth in PBMCs – in contrast, sera from infected individuals could neutralize both PBMC and T-cell line adapted viruses [Beddows1999]					
816	polyclonal	Env	gp120		L	Vaccine	Rhesus macaque
		Vaccine *Vector/Type:* virus-like particle *HIV component:* Pr55gag, anchored gp120, V3+CD4 linear domains **References** Wagner1998b					
		• A VLP is a non-infectious virus-like particle self-assembled from HIV Pr55 gag – macaques were immunized with VLPs bound to either gp120 or V3+CD4 linear domains – Gag and Env specific CTL were stimulated in each case, and Ab response to gag and gp120 and was elicited, but the gp120 neutralizing response occurred only with whole gp120, not V3+CD4 – despite the CTL and Ab response, immunized macaques were infected by intervenous challenge with SHIV chimeric challenge stock [Wagner1998b]					
817	polyclonal	Env	gp120 (IIIB)			Vaccine	murine
		Vaccine *Vector/Type:* DNA *HIV component:* gp120, gp160 **References** Shiver1997					
		• DNA vaccinations of BALBc mice with a gp120 or gp160 DNA vaccine elicited a strong T cell proliferative response with Th1-like secretion of gamma interferon and IL-2, with little or no IL-4, as well as antigen specific gp120 Abs [Shiver1997]					
818	polyclonal	Env	gp120		L	Vaccine	murine
		Vaccine *Vector/Type:* DNA *HIV component:* Gag, Pol, Vif, Env *Adjuvant:* B7, IL-12 **References** Kim1997b					
		• A gag/pol, vif or CMN160 DNA vaccine, when delivered in conjunction with the plasmid encoding the co-stimulatory molecules B7 and IL-12, gave a dramatic increase in both the cytotoxic and proliferative responses in mice – the Ab response was detected by ELISA, but the CMN160 DNA vaccinated mice showed a neutralizing Ab response [Kim1997b]					
819	polyclonal	Env	gp120		P	HIV-1 infection	human
		References Bradney1999					
		• Sera were taken from long term non-progressors and evidence for viral escape was noted – serum could neutralize earlier autologous isolates, but not contemporary isolates [Bradney1999]					
820	polyclonal	Env	gp120		L P	Vaccine	human
		Vaccine *Vector/Type:* canarypox prime with rgp120 boost *Strain:* SF2 *HIV component:* Gag and Env **References** Belshe1998					
		• NAbs were obtained by a HIV-1 gag/env in canary pox vaccination of eight volunteers after boosting with rgp120 against lab strains – 1/8 primary isolates was neutralized, BZ167[Belshe1998]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
821	polyclonal	Env	gp120		L	Vaccine	human

Vaccine *Vector/Type:* canarypox prime with rgp120 boost *Strain:* LAI, MN, SF2 *HIV component:* Gag, Protease, and gp120 *Adjuvant:* MF-59
References Belshe2001

- A phase 2 trial was conducted in 435 volunteers with vCP201, a canary pox vector carrying gp120 (MN in vCP201, and SF2 in the boost), p55 (LAI) and protease (LAI), either alone or with a gp120 boost – NAbs against MN were obtained in 56% of those who received vCP201 alone, and in 94% of those who got the prime with the gp120 boost [Belshe1998]

822	polyclonal	Env	gp120				human (Ig V_H3)

References Neshat2000

- HIV-1 gp120 appears to be a B cell superantigen that binds to members of the V_*H*3 Ig gene family—the gp120 binding site was localized to the Fab portion of the Ab, and discontinuous residues in the V_*H* region were critical [Neshat2000].

823	polyclonal	Env	gp41 (539–684 BH10)			Vaccine	murine (IgG)

Vaccine *Vector/Type:* recombinant protein *HIV component:* gp41
References Bai2000

- Murine rsgp41 antisera recognized a common epitope on human IFNα (aa 29-35 and aa 123-140) and on human IFNβ (aa 31-37 and aa 125-142), suggesting that elevated levels of Ab to IFNs found in HIV+ individuals may be due to a cross-reactive gp41 response [Bai2000].

824	polyclonal	Env	gp120 (BH10)			Vaccine	murine (IgG)

Vaccine *Vector/Type:* DNA *Strain:* ADA, IIIB, 89.6 *HIV component:* gp120 *Adjuvant:* C3d fusion
References Ross2001

- gp120 was fused with murine complement protein C3d in a DNA vaccine to enhance the titers of Ab to Env – fusion to C3d resulted in a more rapid onset of Ab response and avidity maturation, after three immunizations in BALB/c mice with DNA on a gold bead delivered with a gene gun, but not in strong neutralizing Ab response [Ross2001]

825	polyclonal	Env	gp120 (SF162DeltaV2)			Vaccine	Rhesus macaque

Vaccine *Vector/Type:* DNA prime with recombinant protein boost *Strain:* SF162ΔV2 *HIV component:* gp140 *Adjuvant:* MF-59C
References Cherpelis2001b, Cherpelis2001a

- Two animals were immunized both intradermally and intramuscularly at weeks 0, 4, and 8 with a codon optimized DNA vector expressing the SF162V2 gp140 envelope with an intact gp120-gp41 cleavage site, and both developed lymphoproliferative responses and potent neutralizing Abs – CD8+ T lymphocytes were depleted in the animals and they were challenged with SHIV162P4 – at peak viremia, plasma viral levels in the vaccinated animals were 1 to 4 logs lower than those in the unvaccinated animals [Cherpelis2001b]
- HIV-1 SF162ΔV2 gp140 envelope was used in a DNA-prime plus protein-boost vaccination methodology in Rhesus macaques, the animals were depleted of their CD8+ T lymphocytes, and challenged with pathogenic SHIV(SF162P4)—the vaccinated macaques had lower peak viremia, rapidly cleared virus from the periphery, and developed delayed seroconversion to SIV core antigens relative to non-vaccinated controls [Cherpelis2001a].

826	polyclonal	Env	gp120		P	HIV-1 infection	human

References Sarmati2001

- Some HIV-1 infected patients have increasing CD4 counts despite failing ARV, and CD4 levels are correlated with HIV-1 specific NAbs – no correlation was found between NAbs and viral load in this patients [Sarmati2001]

827	polyclonal	Env	gp41 (539–684 BH10)			Vaccine	murine (IgG)

Vaccine *Vector/Type:* recombinant protein *HIV component:* gp41
References Bai2000

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• There is a common epitope in HIV-1 gp41, and IFNalpha and IFNbeta [Bai2000]					
828	polyclonal	Env	gp120 (IIIB)		no		human (IgM)
		References Llorente1999					
		• Combinatorial antibody analysis by phage display and flow cytometry demonstrated that gp120 in HIV-1 negative people is recognized by IgM, but not IgG Abs – IgM Fab reactivity is observed throughout the entire sequence of HIV-1 IIIB gp120 and is characterized by low affinity binding and near germline configuration reflecting a lack of maturation of the IgM repertoire – no neutralizing activity was observed in a non-infected individual before isotope switching [Llorente1999]					
829	polyclonal	Env	gp120 (SF2)		L	Vaccine	human (IgM)
		Vaccine *Vector/Type:* recombinant protein *Strain:* SF2 *HIV component:* gp120					
		References Locher1999					
		• High risk volunteers were vaccinated with SF2 gp120 – 3 breakthrough cases were studied – SF2 neutralizing Abs were observed, but Ab titers to autologous virus were never high and took 6 months after HIV-1 infection to develop – viral loads were similar to HIV-1 infected individuals who had not been vaccinated [Locher1999]					
830	polyclonal	Env	gp120 (subtype A, B, C, D, CRF01)		yes	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* formaldehyde-fixed whole-cell *HIV component:* gp120					
		References LaCasse1999, Nunberg2002					
		• In this study, immunogens were generated that were thought to capture transient envelope-CD4-coreceptor structures that arise during HIV binding and fusion by formaldehyde-fixation of co-cultures of cells expressing HIV-1 Env and those expressing CD4 and CCR5 receptors – these cells elicited NAbs in CD4- and CCR5-transgenic mice that neutralized 23/24 primary isolates from clades A-E [LaCasse1999]					
		• A retraction was printed (Science 296:1025, 2002) noting that an unknown cytotoxic effect of these complex sera accounted for a major fraction of the neutralization reported in [LaCasse1999] [Nunberg2002]					
831	polyclonal	Env	(B consensus)		P	HIV-1 infection	human
		References Morris2001					
		• Ab responses before HAART therapy and after one year of therapy were measured in 8 individuals that were classified HAART successes, and 10 patients who were classified as HAART failures – V3 peptide antibody binding titers to the B-consensus and MN and SF2 variants, and neutralization of HIV-1 MN and four subtype B clinical isolates were tested – subjects with strong anti-V3 and NAb humoral immune responses before starting HAART were more likely to achieve sustained viral suppression to <500 copies RNA/ml on HAART – HIV-specific Ab responses declined after 1 year of successful viral suppression on HAART [Morris2001]					
832	polyclonal	Env			P	HIV-1 infection	human (IgG)
		References Pilgrim1997					
		• Sera from long-term nonprogressors(LTNP) had broader NAbs against heterologous primary isolates and were more likely to neutralize the contemporaneous autologous isolate than were sera from short-term nonprogressors and normal progressors – in 4 individuals followed from acute infection, NAbs were detected against the early autologous isolate by 5-40 weeks, and not detected in an additional 2 cases after 27-45 weeks [Pilgrim1997]					
833	polyclonal	Env			P	HIV-1 infection	human
		References Moog1997					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• Autologous and heterologous NAbs were studied in 18 individuals who were sampled early after sero-conversion and followed longitudinally – autologous NAbs were not detected in sera collected at the same time as the viruses were isolated – NAbs detected against the seroconversion autologous strains were not detected one year after seroconversion, and were highly specific to the virus present at the early phase of HIV infection – heterologous neutralization of primary isolates were not detected until after 2 years [Moog1997]					
834	polyclonal	Env			yes	HIV-1 infection	human
		References Montefiori2001					
		• In 7/9 patients in whom HAART was initiated during early seroconversion, NAbs to autologous strains were not found immediately following treatment interuption after 1-3 years, and Env and Gag Abs were low or undetected by ELISA indicating, that early HAART suppresses the normal antibody response to HIV-1, presumably by limiting the concentration of viral antigens needed to drive B-cell maturation – in 3 patients with a viral rebound autologous NAbs rapidly appeared and correlated with spontaneous down-regulation of viremia – prolonged control of viremia after stopping treatment persisted in the absence of detectable NAbs, suggesting that cellular immune responses alone can control viremia under certain circumstances – these results support the notion that virus-specific B-cell priming, combined with CD8+ CTL induction, may be beneficial for HIV-1 vaccines that aim to suppress viremia in the absence of complete protection to prevent disease and reduce the rate of virus transmission [Montefiori2001]					
835	polyclonal	Env				HIV-1 infection	human (IgG)
		References Scala1999					
		• Random peptide libraries were screened using sera from HIV-infected subjects to identify mimotopes, peptides that mimic conformational or linear epitopes specifically recognized by Abs from HIV-1 infected individuals – the sera of simian SHIV-infected monkeys also recognized the specific peptides, and mice immunized with the selected peptides elicited HIV-specific Abs that neutralized HIV-1 isolates IIIB and NL4-3 [Scala1999]					
836	polyclonal	Env			L	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* peptide *HIV component:* mimotopes					
		References Scala1999					
		• Random peptide libraries were screened using sera from HIV-infected subjects to identify mimotopes, peptides that mimic conformational or linear epitopes specifically recognized by Abs from HIV-1 infected individuals – the sera of simian SHIV-infected monkeys also recognized the specific peptides, and mice immunized with the selected peptides elicited HIV-specific Abs that neutralized HIV-1 isolates IIIB and NL4-3 [Scala1999]					
837	polyclonal	Env				Vaccine	murine (IgG)
		Vaccine *Vector/Type:* virus-like particle *HIV component:* Env, Gag *Adjuvant:* Freund's adjuvant					
		References Lebedev2000					
		• Virus-like particles (VLPs) in the form of spherical particles with yeast dsRNA enveloped in a polysaccharide matrix carrying the protein TBI, that contains fragments of HIV Env and Gag, were used to immunize BALB/c mice and induced specific Abs against HIV-1 as measured by ELISA with TBI [Lebedev2000]					
838	polyclonal	Env			P	HIV-1 infection	human
		References Donners2002					
		• A difference in neutralization patterns between African and European plasma is observed, especially in African women, who tended to have cross-neutralizing Abs against primary isolates [Donners2002].					
839	polyclonal	Env			L	HIV-1 infection	human (IgG)
		References Dianzani2002					
		• Immune complexes(ICs) in the plasma contained HIV RNA (80%-100%) in association with HIV-specific IgG NAbs indicating that the HIV in the plasma of carriers is frequently composed of antibody-neutralized HIV as ICs [Dianzani2002]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
840	polyclonal	Env	Env		P	HIV-1 infection	human (IgG)
		References Kimura2002 • Significant neutralization activity against autologous isolates was observed in 13/19 HIV+ patients at initiation of HAART therapy which persisted during therapy, increasing in one patient, and declining in one patient – 3/6 patients with no detectable NAb at the start of therapy developed NAb responses – of the four patients with increased NAb responses, three had low level viral rebounds (blips) [Kimura2002]					
841	polyclonal	Env			P	HIV-1 exposed seronegative	human (IgA)
		References Devito2000b • Mucosal and plasma HIV-specific IgA that can neutralize primary isolates is present saliva (11/15 tested) and plasma (11/15) and cervicovaginal fluid (11/14) from highly exposed persistently seronegative (HEPS) individuals [Devito2000b]					
842	polyclonal	Env			P	HIV-1 exposed seronegative	human (IgA)
		References Devito2000a • IgA from the genital tract, saliva and plasma from highly exposed persistently seronegative (HEPS) individuals can inhibit transcytosis of HIV-1 across a transwall system that provides a tight epithelial cell layer—50% of the IgA samples studied were able to inhibit transcytosis of at least one of two primary isolates tested, indicating this may be an important mechanism against sexual acquisition of HIV-1 [Devito2000a].					
843	polyclonal	Env			P	HIV-1 exposed seronegative	human (IgA)
		References Broliden2001 • IgA isolated from the saliva, genital tract, and plasma of most highly exposed persistently seronegative (HEPS) sex workers in a Kenyan cohort could neutralize a B, A and D clade primary isolates and could inhibit transcytosis of HIV across a transwall model of the human mucosal epithelium [Broliden2001]					
844	polyclonal	Env			P	HIV-1 exposed seronegative	human (IgA)
		References Devito2002 • IgA isolated from the saliva, genital tract, and plasma of most highly exposed persistently seronegative (HEPS) Kenyan sex workers mediated broad cross-clade neutralization of primary isolates (A, B, C, D, and CRF01) – 6/10 HEPS individuals that were persistently exposed to a stable HIV+ B clade infected partner showed less breadth of neutralization, and were able to neutralize clade A and B primary isolates, but not clades C, D, or CRF01 [Devito2002]					
845	polyclonal	Env			P	HIV-1 exposed seronegative	human (IgA)
		References Mazzoli1999 • Serum HIV-specific IgA is present in highly exposed persistently seronegative individuals (HEPS) in the absence of serum IgG – serum IgA can be found in productively infected individuals and exposed seronegatives at similar titers – 5/15 sera from HEPS had neutralizing activity, 2 of these in purified IgA – HIV-1 specific serum IgA concentrations declined after one year of interruption of at-risk sex [Mazzoli1999]					
846	polyclonal	Env			P	HIV-1 exposed seronegative	human (IgA)
		References Beyrer1999					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• HIV-specific anti-gp160 IgA is present in cervical lavage from 6/13 HIV-exposed seronegative Thai female sex workers [Beyrer1999]					
847	polyclonal	Env				Vaccine	murine
		Vaccine *Vector/Type:* DNA *Strain:* modified HXB2/BaL recombinant **References** Chakrabarti2002 • A modified gp140 (gp140ΔCFI), with C-term mutations intended to mimic a fusion intermediate and stabilize trimer formation, retained antigenic conformational determinants as defined by binding to CD4 and to MAbs 2F5, 2G12, F105, and b12, and enhanced humoral immunity without diminishing the CTL response in mice injected with a DNA vaccine [Chakrabarti2002].					
848	polyclonal	Env				Vaccine	murine
		Vaccine *Vector/Type:* protein *Strain:* IIIB, 89.6 *HIV component:* C4-V3 *Adjuvant:* Freund's adjuvant, alpha2-macroglobin, monophosphoryl lipid A with GMCSF **References** Liao2002 • HIV-envelope peptides coupled to α2-macroglobin were much more immunogenic when formulated in monophosphoryl lipid A with GM-CSF than in complete or incomplete Freund's adjuvant or in monophosphoryl lipid A with GM-CSF alone [Liao2002].					
849	polyclonal	Env	gp120		P	Vaccine	Rhesus macaque
		Vaccine *Vector/Type:* gp120-CD4 complex, gp140-CD4 complex *Strain:* IIIB *HIV component:* gp120, gp140 *Adjuvant:* QS21 **References** Fouts2002 • gp120-CD4 and gp140-CD4 complexes were used for i.m. vaccination of rhesus macaques and neutralizing Ig was recovered using affinity chromatography using a chimeric HIV-BAL gp120 with a mimetic peptide that induces a CD4-triggered mimetic structure – the sera and affinity purified Ab were broadly neutralizing against primary X4, R5, and R5X4 isolates from multiple subtypes but did not react as well against lab-adapted isolates [Fouts2002]					
850	polyclonal	Env			P	HIV-1 infection	human
		References Pastori2002 • HAART initiated during primary infection was studied in seven patients and had different effects on NAb production—in some cases, α-Env Abs were inhibited during primary infection, and in some cases strong NAbs against autologous virus were induced [Pastori2002].					
851	polyclonal	Env	gp120		L	HIV-1 infection	chimpanzee (IgG)
		References Igarashi1999, Moore1999 • The rate of virus clearance in the circulation in rhesus macaques receiving a continuous infusion of cell-free viral dual-tropic virus isolate HIV-1DH12 particles in the presence and absence of virus-specific antibodies was measured – the clearance of physical and infectious viral particles is very rapid in naive animals, with half-lives ranging from 13 to 26 minutes, but clearance cold be acheived with a half life of 3.9-7.2 minutes when chimpanzee neutralizing Abs were present to help to remove virions from the blood [Igarashi1999] • polyclonal: Commentary discussing this finding noting the particularly high neutralization titer and limited breadth of the chimpanzee sera used in this study [Moore1999]					
852	polyclonal	Env	gp120		L	Vaccine	human
		Vaccine *Vector/Type:* canarypox prime with rgp120 boost *Strain:* gp120 MN and gp41 LAI, rgp120 SF2 *Adjuvant:* MF-59 **References** Gupta2002 • Vaccine trial protocol 022A in 150 HIV-1 uninfected adults (130 completed the study) showed high titer ALVAC vaccine in combination with gp120 was safe and immunogenic in HIV-1 negative volunteers – NAb responses were detected in 95% of vaccinees, with higher titers in recipients of sequential versus simultaneous dosing of the two vaccines and in vaccinia naive volunteers [Gupta2002]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
853	101-342	Env	gp120 (476–505 HAM112, O group)			Vaccine	murine (IgG2a κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* HAM112 (group O) *HIV component:* gp160 **Ab type** C-term **References** Scheffel1999 • 101-342: Overlapping peptides based on group O HAM112 Env were tested for MAb reactivity [Scheffel1999]					
854	101-451	Env	gp120 (498–527 HAM112, O group)			Vaccine	murine (IgG2b κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* HAM112 (group O) *HIV component:* gp160 **Ab type** C-term **References** Scheffel1999 • 101-451: Overlapping peptides based on group O HAM112 Env were tested for MAb reactivity [Scheffel1999]					
855	120-1	Env	gp120 (503–532)		no	Vaccine	murine (IgMκ)
		Vaccine *Vector/Type:* peptide **Ab type** C-term **References** Chanh1986, Dalgleish1988					
856	212A	Env	gp120		no	HIV-1 infection	human
		Ab type C1 **Donor** James Robinson, Tulane University, LA **References** Robinson1992, Moore1994d, Moore1996, Binley1997a, Fouts1997, Ditzel1997, Wyatt1997, Parren1997c, Sullivan1998b, Binley1998 • 212A: Mutations that inhibit binding: C1 (45 W/S) and V5 (463 N/D) – and enhance binding: V2 (179/180 LD/DL) and C5 (495 G/K) [Moore1994d] • 212A: Binding enhanced by anti-V3 MAb 5G11 – reciprocal inhibition with anti-C1 MAbs [Moore1996] • 212A: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric Env binding – 212A bound monomer, did not bind oligomer or neutralize JRFL [Fouts1997] • 212A: Binds efficiently to sgp120 but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding – does not bind to HXBc2 gp120 if the 19 C-term amino acids are deleted [Wyatt1997] • 212A: Does not neutralize TCLA strains or primary isolates [Parren1997c] • 212A: Does not compete with binding of MAb generated in response to gp120-CD4 complex, CG10 [Sullivan1998b] • 212A: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer [Binley1998]				
857	522-149	Env	gp120		no	Vaccine	
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Env **Ab type** C1 **Donor** G. Robey, Abbott Inc. **References** Moore1996, Trkola1996a, Binley1998, Yang2000 • 522-149: Binding is enhanced by C5 antibodies M91 and 1C1 – mutual binding-inhibition with anti-C1 antibody 133/290 – binding is destroyed by a W/L (position 61, LAI) gp120 amino acid substitution – other C1 antibodies enhance binding to gp120 [Moore1996] • 522-149: Does not neutralize JR-FL nor block gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study [Trkola1996a] • 522-149: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer [Binley1998]				

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 522-149: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) that preserve and expose some neutralizing epitopes while occluding some non-neutralizing epitopes – CD4BS MAbs (F105 and F91) and CD4i (17b and 48d) recognized gp140-GNC4 as well as gp120 or gp140 – non-neutralizing MAbs C11, A32, 522-149, M90, and #45 bound to the gp140-GNC4 glycoprotein at reduced levels compared to gp120 – MAbs directed at the extreme termini of gp120 C1 (135/9 and 133/290) and C5 (CRA-1 and M91) bound efficiently to gp140-GNC4 [Yang2000]				
858	L19	Env	gp120 (HXBc2)			HIV-1 infection	human Fab (IgG1)
		Ab type C1 **References** Ditzel1997 • L19: gp120 immobilized on solid phase by capture with anti-CD4 BS MAb L72 was used for the selection of Fabs – six N-term Fabs, L19 L34, L35, L52, L59, and L69, were obtained that have a similar epitope to Fab p7 [Ditzel1997]					
859	M90	Env	gp120		no	Vaccine	(IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* Env **Ab type** C1 **Donor** Fulvia di Marzo Veronese **References** diMarzo Veronese1992, DeVico1995, Moore1996, Ditzel1997, Wyatt1997, Binley1998, Binley1999 • M90: Reactive only with native gp120, so binds to a discontinuous epitope – reacts with multiple strains [diMarzo Veronese1992] • M90: Reacted with both non-reduced (but not denatured) covalently cross-linked gp120-CD4 complex [DeVico1995] • M90: Reciprocal inhibition of binding of other anti-C1 MAbs – inhibits CD4 binding site MAbs – enhances binding of V2 MAbs G3-4 and SC258 [Moore1996] • M90: Binds efficiently to sgp120 but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding – does not bind to HXBc2 gp120 if the 19 C-term amino acids, in conjunction with C1 positions 31-82, are deleted [Wyatt1997] • M90: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer [Binley1998] • M90: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes [Binley1999] • M90: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) that preserve and expose some neutralizing epitopes while occluding some non-neutralizing epitopes – CD4BS MAbs (F105 and F91) and CD4i (17b and 48d) recognized gp140-GNC4 as well as gp120 or gp140 – non-neutralizing MAbs C11, A32, 522-149, M90, and #45 bound to the gp140-GNC4 glycoprotein at reduced levels compared to gp120 – MAbs directed at the extreme termini of gp120 C1 (135/9 and 133/290) and C5 (CRA-1 and M91) bound efficiently to gp140-GNC4 [Yang2000]			
860	MAG 104	Env	gp120		no	Vaccine	murine
		Vaccine *Vector/Type:* sCD4-gp120 complex *Strain:* HXB2 *HIV component:* gp120 **Ab type** C1 **Donor** C. Y. Kang, IDEC Inc **References** Kang1994 • MAG 104: Only observed amino acid substitution that reduces binding: 88 N/P and 106 E/A – does not bind to C1 region 20 mer peptides, tentative classification conformationally sensitive anti-C1 MAb [Kang1994]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
861	MAG 45 (#45)	Env	gp120		no	Vaccine	murine

Vaccine *Vector/Type:* sCD4-gp120 complex *Strain:* HXB2 *HIV component:* gp120
Ab type C1 **Donor** C. Y. Kang, IDEC Inc
References Kang1994, Moore1996, Wyatt1997, Yang2000

- MAG 45: Only observed amino acid substitution that reduces binding: 88 N/P – does not bind to C1 region 20 mer peptides, tentative classification conformationally sensitive anti-C1 MAb [Kang1994]
- MAG 45: Reciprocal binding inhibition with anti-C1-C5 and anti-C1-C4 discontinuous MAbs – binding enhanced by anti-V3 5G11 – inhibits binding of anti-CD4 binding site MAbs [Moore1996]
- MAG 45: Called #45 – binds to efficiently sgp120 but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding – does not bind to HXBc2 gp120 if the 19 C-term amino acids, in conjunction with C1 positions 31-50, are deleted [Wyatt1997]
- MAG 45: Called #45 – a combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) that preserve and expose some neutralizing epitopes while occluding some non-neutralizing epitopes – CD4BS MAbs (F105 and F91) and CD4i (17b and 48d) recognized gp140-GNC4 as well as gp120 or gp140 – non-neutralizing MAbs C11, A32, 522-149, M90, and #45 bound to the gp140-GNC4 glycoprotein at reduced levels compared to gp120 – MAbs directed at the extreme termini of gp120 C1 (135/9 and 133/290) and C5 (CRA-1 and M91) bound efficiently to gp140-GNC4 [Yang2000]

862	MAG 95	Env	gp120		no	Vaccine	murine

Vaccine *Vector/Type:* sCD4-gp120 complex *Strain:* HXB2 *HIV component:* gp120
Ab type C1 **Donor** C. Y. Kang, IDEC Inc
References Kang1994

- MAG 95: Only observed amino acid substitution that reduces binding: 88 N/P – does not bind to C1 region 20 mer peptides, tentative classification conformationally sensitive anti-C1 MAb [Kang1994]

863	MAG 97	Env	gp120		no	Vaccine	murine

Vaccine *Vector/Type:* sCD4-gp120 complex *Strain:* HXB2 *HIV component:* gp120
Ab type C1 **Donor** C. Y. Kang, IDEC Inc
References Kang1994

- MAG 97: Only observed amino acid substitution that reduces binding: 88 N/P – does not bind to C1 region 20 mer peptides, tentative classification conformationally sensitive anti-C1 MAb [Kang1994]

864	T9	Env	gp41			Vaccine	murine (IgG)

Ab type C1 **Donor** Patricia Earl and Christopher Broder, NIH
References Broder1994, Earl1997, Golding2002b

- There are two HIV-Abs with the name T9, one binds to gp41, one to gp120
- T9: One of five MAbs (T4, T6, T9, T10 and T35) in a competition group that bind to a conformation-dependent epitope in gp41 and is oligomer specific – neutralizes IIIB and SF2 [Broder1994]
- T9: This antibody, along with 7 others (M10, D41, D54, T6, T4, T10 and T35), can block the linear murine MAb D61, and the human MAb 246-D, which both bind to the immunodominant region near the two Cys in gp41 – most of these antibodies are oligomer dependent – all of the MAbs are reactive with ten different HIV-1 strains – members of this competition group are blocked by sera from HIV-1+ individuals [Earl1997]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• T9: The fusion process was slowed by using a suboptimal temperature (31.5 C) to re-evaluate the potential of Abs targeting fusion intermediates to block HIV entry – preincubation of E/T cells at 31.5 C enabled polyclonal anti-N-HR Ab and anti-six-helix bundle Abs to inhibit fusion, indicating six-helix bundles form prior to fusion – the preincubation 31.5 C step did not alter the inhibitory activity of neutralizing Abs anti-gp41 2F5, or anti-gp120 2G12, IG1b12, 48d, and 17b – nor did it alter two gp41 MAbs, T9 and D61, inability to inhibit fusion [Golding2002b]				
865	p7	Env	gp120 (HXBc2)			HIV-1 infection	human Fab (IgG1)
		Ab type C1 **References** Ditzel1997, Parren1997c • p7: gp120 immobilized on solid phase by capture with sCD4 was used for selection of Fabs – three novel N-term Fabs were obtained that bind to similar epitopes, p7, p20, and p35 – a C1 W/S substitution at position 45 abolished binding, a Y/D at position 45 reduced binding, and C5 region substitutions 475 M/S and 493 P/K enhanced binding – compete with MAbs M85, M90 and 212A, but not M91 and G3-299 [Ditzel1997] • p7: Does not neutralize TCLA strains or primary isolates [Parren1997c]				
866	L100	Env	gp120 (HXBc2)			HIV-1 infection	human Fab (IgG1)
		Ab type C1-C2 **References** Ditzel1997, Parren1997c, Parren1997a • L100: Does not neutralize TCLA strains or primary isolates [Parren1997c] • L100: gp120 immobilized on solid phase by capture with sCD4 and then masked with Fab p7 allowed selection of a new Fab, L100, with a novel specificity for C1 and C2 – gp120 C1 substitutions 69 W/L and 76 P/Y abolish L100 binding, and C2 substitutions 252 R/W, 256 S/Y, 262 N/T and 267 E/L abolish or strongly inhibit L100 binding – inhibits binding of MAbs M90 and G3-299, but not M85, 212A, and M91 [Ditzel1997, Parren1997a]				
867	2/11c (211c, 2.11c, 211/c, 2-11c)	Env	gp120		L (weak)	HIV-1 infection	human
		Ab type C1-C4 **Donor** James Robinson, Tulane University, LA **References** Moore1996, Trkola1996a, Binley1997a, Fouts1997, Li1997, Wyatt1997, Binley1998, Xiang2002a • 2/11c: Inhibits binding of anti-C1, -C5, -C4, -V3 and anti-CD4 binding site MAbs – induces binding of some anti-V2 and CD4i MAbs (48d and 17b) – similar reactivity pattern to A32, but less cross-reactive and lower affinity – A32 and 211/c are unique among known human and rodent MAbs [Moore1996] • 2/11c: Called 211c – does not neutralize JR-FL nor block gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study [Trkola1996a] • 2/11c: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric env binding – 2/11c bound monomer, did not bind oligomer or neutralize JRFL [Fouts1997] • 2/11c: Called 2.11c – One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB env – 50% neutralization could not be achieved at a maximal concentration of 67 mug/ml [Li1997] • 2/11c: Binds efficiently to sgp120 but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding – does not bind to HXBc2 gp120 if the 19 C-term amino acids, in conjunction with C1 positions 31-74, are deleted [Wyatt1997] • 2/11c: Called 211/c – a panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer [Binley1998] • 2/11c: Used as a negative control in a study of CD4i MAbs [Xiang2002a]				
868	A32	Env	gp120		no	HIV-1 infection	human (IgG1)
		Ab type C1-C4 **Donor** James Robinson, Tulane University, New Orleans, LA, USA **References** Moore1994b, Wyatt1995, Moore1995b, Moore1996, Wu1996, Trkola1996a, Binley1997a, Fouts1997, Burton1997, Wyatt1997, Boots1997, Parren1997c, Sullivan1998b, Binley1998, Binley1999, Yang2000, Yang2002, Grundner2002 • A32: Reacted with virtually every gp120 monomer of every clade tested, most conserved gp120 monomer epitope known [Moore1994b]				

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- A32: Epitope is better exposed upon CD4 binding to gp120 – binding of A32 enhances binding of 48d and 17b – studies using a V1/V2 deletion mutant demonstrated that enhanced binding of 48d in the presence sCD4 involves the V1/V2 loops, with more significant involvement of V2 [Wyatt1995]
- A32: Review: epitope is distinct from CD4BS MAbs, 48d and 17b, and 2G12 [Moore1995b]
- A32: Reciprocal inhibition of binding of anti-C1, -C5, -C4, -V3 and anti-CD4 binding site MAbs – induces binding of some anti-V2 and sCD4 inducible MAbs (48d and 17b) – very similar competition pattern to 2/11c, A32 and 211/c are unique among known human and rodent MAbs [Moore1996]
- A32: Not neutralizing – binds domains that interact with gp41 – MIP-1alpha binding to CCR-5 expressing cells can be inhibited by gp120-sCD4 and binding of A32 does not block this inhibition [Wu1996]
- A32: Does not neutralize JR-FL, or any strain strongly – partial inhibition of gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study [Trkola1996a]
- A32: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric env binding – A32 bound monomer, did not bind oligomer or neutralize JRFL [Fouts1997]
- A32: Review [Burton1997]
- A32: Binds efficiently to sgp120 but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding [Wyatt1997]
- A32: Does not neutralize TCLA strains or primary isolates [Parren1997c]
- A32: Abs that recognize discontinuous epitopes can identify mimotopes from a phage peptide display library – A32 has a unique epitope involving mostly C2 but C1 and C4 contribute – six quite variable phage inserts were recognized, with a consensus of LPWYN – a central Trp was the most conserved element, consistent with W427 being an important residue for binding gp120 [Boots1997]
- A32: Enhances binding of CD4i MAbs 17b and 48d, and a MAb generated in response to gp120-CD4 complex, CG10 [Sullivan1998b]
- A32: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer [Binley1998]
- A32: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes [Binley1999]
- A32: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) that preserve and expose some neutralizing epitopes while occluding some non-neutralizing epitopes – CD4BS MAbs (F105 and F91) and CD4i (17b and 48d) recognized gp140-GNC4 as well as gp120 or gp140 – non-neutralizing MAbs C11, A32, 522-149, M90, and #45 bound to the gp140-GNC4 glycoprotein at reduced levels compared to gp120 – MAbs directed at the extreme termini of gp120 C1 (135/9 and 133/290) and C5 (CRA-1 and M91) bound efficiently to gp140-GNC4 [Yang2000]
- A32: Uncleaved soluble gp140 (YU2 strain, R5 primary isolate) can be stabilized in an oligomer by fusion with a C-term trimeric GCN4 motif or using a T4 trimeric motif derived from T4 bacteriophage fibritin – stabilized oligomer gp140 delta683(-FT) showed strong preferential recognition by NAbs IgG1b12 and 2G12 relative to the gp120 monomer, in contrast to poorly neutralizing MAbs F105, F91, 17b, 48d, and 39F which showed reduced levels of binding, and C11, A32, and 30D which did not bind the stabilized oligomer [Yang2002]
- A32: HIV-1 gp160deltaCT (cytoplasmic tail-deleted) proteoliposomes (PLs) containing native, trimeric envelope glycoproteins from R5 strains YU2 and JRFL, and X4 strain HXBc2, were made in a physiologic membrane setting as candidate immunogens for HIV vaccines – 2F5 bound to gp160deltaCT with a reconstituted membrane ten-fold better than the same protein on beads – anti-CD4BS MAbs IgG1b12 and F105, A32 (C1-C4), C11 (C1-C5), and 39F (V3) MAbs bound gp160deltaCT PLs indistinguishably from gp160deltaCT expressed on the cell surface – non-neutralizing MAbs C11 and A32 bound with lower affinity than NAb IgG1b12 – the MAb 17b was sCD4 inducible on gp160deltaCT PL [Grundner2002]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
869	C11 (c11)	Env	gp120		no	HIV-1 infection	human

Ab type C1-C5 **Donor** James Robinson, Tulane University, LA

References Robinson1992, Moore1994d, Moore1996, Trkola1996a, Wu1996, Binley1997a, Fouts1997, Wyatt1997, Parren1997c, Sullivan1998b, Binley1999, Yang2002, Grundner2002, Basmaciogullari2002

- C11: Mutations that inhibit binding: C1 (45 W/S, 88 N/P) – V5 (463 N/D) – and C5 (491 I/F, 493 P/K and 495 G/K) and enhance binding: C1 (36 V/L) – V1-V2 (152/153 GE/SM) – and DeltaV1/V2/V3 [Moore1994d]
- C11: Binding enhanced by anti-V3 MAb 5G11 – reciprocal inhibition with anti-C1 MAbs [Moore1996]
- C11: Did not block ability of gp120-sCD4 complexes to inhibit MIP-1alpha binding – binds to gp41-binding domain [Wu1996]
- C11: Does not neutralize JR-FL nor block gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study [Trkola1996a]
- C11: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric Env binding – C11 bound monomer, did not bind oligomer or neutralize JRFL [Fouts1997]
- C11: Binds efficiently to sgp120 but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding – partial re-exposure if sCD4 was bound – does not bind to HXBc2 gp120 if the 19 C-term amino acids are deleted [Wyatt1997]
- C11: Does not neutralize TCLA strains or primary isolates [Parren1997c]
- C11: Does not compete with binding of MAb generated in response to gp120-CD4 complex, CG10 [Sullivan1998b]
- C11: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes [Binley1999]
- C11: Uncleaved soluble gp140 (YU2 strain, R5 primary isolate) can be stabilized in an oligomer by fusion with a C-term trimeric GCN4 motif or using a T4 trimeric motif derived from T4 bacteriophage fibritin – stabilized oligomer gp140 delta683(-FT) showed strong preferential recognition by NAbs IgG1b12 and 2G12 relative to the gp120 monomer, in contrast to poorly neutralizing MAbs F105, F91, 17b, 48d, and 39F which showed reduced levels of binding, and C11, A32, and 30D which did not bind the stabilized oligomer [Yang2002]
- C11: HIV-1 gp160deltaCT (cytoplasmic tail-deleted) proteoliposomes (PLs) containing native, trimeric envelope glycoproteins from R5 strains YU2 and JRFL, and X4 strain HXBc2, were made in a physiologic membrane setting as candidate immunogens for HIV vaccines – 2F5 bound to gp160deltaCT with a reconstituted membrane ten-fold better than the same protein on beads – anti-CD4BS MAbs IgG1b12 and F105, A32 (C1-C4), C11 (C1-C5), and 39F (V3) MAbs bound gp160deltaCT PLs indistinguishably from gp160deltaCT expressed on the cell surface – non-neutralizing MAbs C11 and A32 bound with lower affinity than NAb IgG1b12 – the MAb 17b was sCD4 inducible on gp160deltaCT PL [Grundner2002]
- C11: gp120 mutants were used to define the CXCR4 binding site using CXCR4 displayed on paramagnetic proteoliposomes (PMPLs) to reduce non-specific gp120 binding – basic residues in the V3 loop and the beta19 strand (RIKQ, positions 419-422) were involved, and deletion of the V1-V2 loops allowed CD4-independent CXCR4 binding – MAbs 17b (CD4i) and F105 (CD4BS) were used to study conformational changes in the mutants – C11 was used to detect gp120 binding to CXCR4 or CCR5 on PMPLs [Basmaciogullari2002]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
870	L81	Env	gp120		no	HIV-1 infection	human (IgG1)

Ab type C1-C5

References Ditzel1997, Parren1997c

- L81: gp120 immobilized on solid phase by capture with anti-CD4 BS MAb L72 was used for selection of Fabs – L81 binding is abolished by C1 substitution 45 W/S, C5 substitution 491 I/F, and C3 substitution L/A [Ditzel1997]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• L81: Does not neutralize TCLA strains or primary isolates [Parren1997c]					
871	2F19C	Env	gp120 (HIV2ROD)	APGK	no	Vaccine	murine
		Vaccine *Vector/Type:* peptide *Strain:* HIV-2 ROD **Ab type** C3 **References** Matsushita1995 • 2F19C: Binds in WB, but binds poorly to Env on the cell surface, APGK is the core binding region [Matsushita1995]					
872	B2C	Env	gp120 (HIV2ROD)	HYQ(core)	L	Vaccine	murine
		Vaccine *Vector/Type:* peptide *Strain:* HIV-2 ROD **Ab type** C3 **References** Matsushita1995 • B2C: Viral neutralization was type-specific for HIV-2 ROD [Matsushita1995]					
873	polyclonal	Env			P	HIV-1 infection	human (IgG)
		Ab type C3 **References** Wang2002a • Autologous NAbs were studied in 3 patients on HAART that rebounded – phylogenetic analysis of env (V1-V5) sequences indicated that rebound viruses had evolved from or preexisted in baseline populations – HIV-1 rebound viruses from all 3 patients were resistant to neutralization by autologous IgG, unlike the baseline viruses – mutations in the C3 region was responsible for conferring neutralization resistance against autologous antibody in 2 of 3 patients [Wang2002a]					
874	1024	Env	gp120				
		Ab type C4 **References** Berman1997 • 1024: Binds to 1/7 isolates from breakthrough cases from a MN gp120 vaccine trial [Berman1997]					
875	23A (2.3A)	Env	gp120		no		
		Ab type C5 **Donor** James Robinson, Tulane University, LA **References** Thali1992a, Thali1993, Wu1996, Trkola1996a, Fouts1997, Binley1999, Schulke2002 • 23A: Called 2.3A – Did not block ability of gp120-sCD4 complexes to inhibit MIP-1alpha binding – binds to gp41-binding domain of gp120 [Wu1996] • 23A: C5 binding MAb – does not inhibit gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study [Trkola1996a] • 23A: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric env binding – 23A bound monomer, did not bind oligomer or neutralize JRFL [Fouts1997] • 23A: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes [Binley1999] • 23A: Ab binding characteristics of SOS gp140 were tested using SPR and RIPA – SOS gp140 is gp120-gp41 bound by a disulfide bond – NAbs 2G12, 2F5, IgG1b12, CD4 inducible 17b, and 19b bound to SOS gp140 better than uncleaved gp140 (gp140unc) and gp120 – non-neutralizing MAbs 2.2B (binds to gp41 in gp140unc) and 23A (binds gp120) did not bind SOS gp140 [Schulke2002]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
876	D7324	Env	gp120			Vaccine	sheep

Vaccine *HIV component:* gp120
Ab type C5 **Donor** Aalto BioReagents Ltd, Dublin, Ireland or Cliniqa Inc., Fallbrook, CA, USA
References Moore1990a, Sattentau1991, Moore1993b, Moore1993c, Wyatt1995, Trkola1996a, Ditzel1997, Ugolini1997, Mondor1998, Binley1998, Sanders2002, Gram2002, Xiang2002a, Basmaciogullari2002, Poignard2003, Herrera2003

- D7324: Binding unaltered by gp120 binding to sCD4, in contrast to 110.5, 9284, 50-69 and 98-6 [Sattentau1991]
- D7324: Binds to the last 15 amino acids in gp120 – used for antigen capture ELISA [Wyatt1995]
- D7324: Epitope in C5 – Does not neutralize JR-FL nor block gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study [Trkola1996a]
- D7324: Called NEA9205 – gp120 capture ELISAs with MAbs D7324 (anti-C-term) or 9205 (anti-V3) were compared in a study of orientation of glycosylation sites – CD4 binding could only inhibit deglycosylation when gp120 was bound to the plate by D7324, not by 9205, while Abs from HIV-1 infected people inhibited deglycosylation most effectively when gp120 was caught by 9205 [Gram2002]
- D7324: Used to capture gp120 onto solid phase for epitope mapping [Moore1993b], [Moore1993c], [Ditzel1997], [Binley1998], [Sanders2002], [Xiang2002a], [Basmaciogullari2002], [Poignard2003], [Herrera2003]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
877	10/46c	Env	gp120			Vaccine	rat

Vaccine *Vector/Type:* recombinant protein *HIV component:* gp120
Ab type CD4BS
References Cordell1991, Jeffs1996, Peet1998

- 10/46c: Increased binding when V1/V2 or V1/V2 and V3 were deleted from gp120 [Jeffs1996]
- 10/46c: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind – 10/46c was not affected by V3 serine substitutions – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions [Peet1998]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
878	1027-30-D	Env	Env				human (IgG1κ)

Ab type CD4BS **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Hioe2000

- 1027-30-D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – anti-CD4 binding site MAbs or serum Ig from HIV+ individuals inhibited proliferative responses of gp120 specific T cells – CD4BS MAbs 654-D, 559/64-D, 588-D, 830-D, 1027-30-D, and 1202-30D strongly diminished proliferation [Hioe2000]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
879	1125H (1125h)	Env	gp120		L (MN)	HIV-1 infection	human (IgG1κ)

Ab type CD4BS **Donor** Shermaine Tilley, Public Health Research Institute, USA
References
Tilley1991a, Tilley1991b, Thali1992a, Wyatt1992, Pinter1993b, D'Souza1995, Warrier1996, Pincus1996, Wyatt1998a, Alsmadi1998, Yang1998

- 1125H: Binding to gp120 inhibited by CD4 – epitope is destroyed by reduction, but not by removal of N-linked sugars – potent neutralization of MN, RF, SF-2 and IIIB – neutralization synergy with anti-V3 MAb 4117C [Tilley1991b]
- 1125H: Amino acid substitutions in HXB2 that strongly inhibit binding: 88, 102, 117, 113, 257, 368, 370, 421, 427, 457, 470, 480 [Thali1992a]
- 1125H: Binding to soluble gp120 enhanced by the presence of an anti-V3 HuMAb, 41148D [Pinter1993b]
- 1125H: Precipitation of Delta 297-329 env glycoprotein, with has a deleted V3 loop, is much more efficient that precipitation of wild type [Wyatt1992]
- 1125H: Neutralization was MN specific – failed to neutralize JRCSF, and 2 B subtype and 1 D subtype primary isolates in a multi-laboratory study involving 11 labs [D'Souza1995]
- 1125H: Synergistic neutralization of HIV-1 when combined with anti-V2 MAb C108G [Warrier1996]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 1125H: A panel of immunotoxins were generated by linking Env MAbs to ricin A – immunotoxins mediated cell killing, but killing was not directly proportional to binding [Pincus1996] • 1125H: Called 1125h – summary of the implications of the crystal structure of the core of gp120 bound to CD4 and 17b with what is known about mutations that reduce NAb binding – probable mechanism of neutralization by CD4BS Ab is direct interference with CD4 binding [Wyatt1998a] • 1125H: A study of 6 anti-Env MAbs and their ability to bind or direct ADCC against target cells infected with IIIB, MN, SF-2, and RF – bound and directed lysis against all four strains [Alsmadi1998] • 1125H: A neutralization assay was developed based on hemi-nested PCR amplification of the LTR (HNPCR) – LTR-HNPCR consistently revealed HIV DNA and was shown to be a rapid, specific and reliable neutralization assay based on tests with 6 MAbs and 5 isolates [Yang1998]				
880	120-1B1	Env	gp120		L		human
		Ab type CD4BS **Donor** Virus Testing Systems Corp., Houston, TX **References** Watkins1993 • 120-1B1: A neutralization escape mutant (HXB2 A281V) was selected by growth of HXB2 in the presence of broadly neutralizing sera – 120-1B1 was not affected by this mutation [Watkins1993]					
881	1202-D (1202-30-D)	Env	Env				human (IgG1κ)
		Ab type CD4BS **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center) **References** Nyambi1998, Hioe2000, Nyambi2000 • 1202-D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – CD4-BS Abs tended to bind weakly without clade specificity to virions, but bound well to soluble gp120 – 1202-D did not bind to any B clade viruses, and weakly bound A, C, and G clade isolates – 559/64-D, 558-D and 1202-D had similar reactivities [Nyambi1998] • 1202-D: Called 1202-30D – Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – anti-CD4 binding site MAbs or serum Ig from HIV+ individuals inhibited proliferative responses of gp120 specific T cells – CD4BS MAbs 654-D, 559/64-D, 588-D, 830-D, 1027-30-D, and 1202-30D strongly diminished proliferation [Hioe2000] • 1202-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 CD4BS MAbs – CD4BS MAbs bound consistently to most isolates of clade D, but poorly to isolates of other clades with the exception of broadly reactive MAb IgG1b12[Nyambi2000]				
882	1331E	Env	gp120 (IIIB)			HIV-1 infection	human (IgG1κ)
		Ab type CD4BS **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center) **References** Gorny2000a • 1331E: Inhibits sCD4 binding to rec gp120 LAI – binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – CD4BS MAbs 559/64-D, 654-D, 729-D, 9CL and 1331E bound with a 5-13 fold preference for the oligomer [Gorny2000a]				
883	1570 (1570A, 1570C, 1570D)	Env	Env (PR12, BH10)			HIV-1 infection	human
		Ab type CD4BS **References** Jeffs2001 • 1570: BH10 was mutated to form the PR12 protein with the first 74 C-terminal amino acids and the V1, V2 and V3 hypervariable loops deleted and a very well exposed CD4 binding domain (CD4bd) – this proteins was used to select three new human CD4BS MAbs 1570, 1595 and 1599 – three MAbs were isolated from one individual, 1570A, C and D but all were determined to have the same V(H)3 region – 1570 was able to bind to a panel of recombinant proteins from the A, B, C, D, and E subtypes [Jeffs2001]				
884	1595	Env	Env (PR12, BH10)			HIV-1 infection	human
		Ab type CD4BS					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

References Jeffs2001

- 1595: BH10 was mutated to form the PR12 protein with the first 74 C-terminal amino acids and the V1, V2 and V3 hypervariable loops deleted and a very well exposed CD4 binding domain (CD4bd) – this proteins was used to select three new human CD4BS MAbs 1570, 1595 and 1599 – 1595 was able to bind gp120 from the A, B, and D clades from a panel of recombinant proteins from the A, B, C, D, and E subtypes [Jeffs2001]

885	1599	Env	Env (PR12, BH10)			HIV-1 infection	human

Ab type CD4BS

References Jeffs2001

- 1599: BH10 was mutated to form the PR12 protein with the first 74 C-terminal amino acids and the V1, V2 and V3 hypervariable loops deleted and a very well exposed CD4 binding domain (CD4bd) – this proteins was used to select three new human CD4BS MAbs 1570, 1595 and 1599 – 1599 was able to bind gp120 only from the B clade from a panel of recombinant proteins from the A, B, C, D, and E subtypes [Jeffs2001]

886	15e (1.5e, 1.5E, 15E)	Env	gp120		L	HIV-1 infection	human (IgG1κ)

Ab type CD4BS **Donor** James Robinson, Tulane University, LA, and David Ho, ADARC, NY, NY

References Robinson1990a, Thali1991, Cordell1991, Ho1991b, Koup1991, Ho1992, Wyatt1992, Thali1992a, Takeda1992, Moore1993a, Thali1993, Wyatt1993, Bagley1994, Thali1994, Cook1994, Moore1994b, Moore1994a, Sattentau1995b, Lee1995, McKeating1996b, Moore1996, Poignard1996a, Trkola1996a, McDougal1996, Wisnewski1996, Binley1997a, Fouts1997, Li1997, Wyatt1997, Berman1997, Parren1997c, Wyatt1998a, Parren1998a, Sullivan1998b, Binley1998, Trkola1998, Fouts1998, Sullivan1998a, Park2000, Kolchinsky2001, Xiang2002b, Zhang2002, Pantophlet2003

- 15e: Broadly neutralizing, binds multiple strains, competes with CD4 for gp120 binding, DTT reduction of env abrogates binding – more potent blocking of gp120-sCD4 binding than MAbs G3-536 and G3-537 [Ho1991b]
- 15e: Cross-competes with MAbs ICR 39.13g and ICR 39.3b [Cordell1991]
- 15e: Binds to gp120 of HIV-1 IIIB, but not RF – mediates ADCC – deletion of the V3 loop from gp120 does not alter ADCC activity [Koup1991]
- 15e: gp120 mutants that affect 15e epitope binding: 113, 257, 368, 370, 421, 427, 475 – four of these coincide with amino acids important for the CD4 binding domain [Ho1992]
- 15e: Precipitation of Delta 297-329 env glycoprotein, with a deleted V3 loop, is much more efficient that precipitation of wild type [Wyatt1992]
- 15e: Amino acid substitutions in HXB2 that strongly inhibit binding, similar to [Ho1992], some additional, 88, 102, 117, 113, 257, 368, 370, 421, 427, 457, 470, 480 [Thali1992a]
- 15e: Called N70-1.5e – does not enhance infection of HIV-1 IIIB and MN [Thali1992a]
- 15e: Conformational, does not bind denatured gp120 – neutralizes IIIB – reactive with SF-2 gp120 – strong inhibition of HIV+ human sera binding to IIIB gp120 [Moore1993a]
- 15e: Binding to Delta V1/2 and Delta V1/2/3 mutant glycoproteins is greater than binding to wildtype gp120 [Wyatt1993]
- 15e: Called 15E – a neutralization escape mutant (HXB2 A281V) was selected by growth of HXB2 in the presence of broadly neutralizing sera – 15E neutralization was not affected by this mutation [Watkins1993]
- 15e: Heavy chain is V HIV, V2-1 – light chain is V_kappaI, Hum01/012. Compared to 21h and F105 [Bagley1994]
- 15e: A mutation in gp41, 582 A/T, confers resistance to neutralization (also confers resistance to MAbs F105, 48d, 21h and 17b) [Thali1994]
- 15e: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – anti-CD4 MAbs moderately inhibit gp120 binding to GalCer, possibly through steric hindrance – binding of GalCer to gp120 inhibited but did not completely block 15e binding [Cook1994]
- 15e: Cross-reactive with gp120 proteins from clades B and D, less so with A and C, and not reactive with clade E and F [Moore1994b]
- 15e: Binds with higher affinity to monomer than to oligomer, moderate association rate [Sattentau1995b]
- 15e: The V4 and V5 domains are essential for 1.5e binding, in contrast to the V1, V2, and V3 loops [Lee1995]
- 15e: Called 1.5e – Neutralizes HXB2, but fails to neutralize chimeric virus with gp120 from primary isolates in an HXB2 background [McKeating1996b]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 15e: gp120 binding enhanced by anti-V3 MAb 5G11 and anti-V2 MAb G3-136 – binding inhibited by other CD4 binding site MAbs, antibodies that bind to gp120 only when CD4 is bound, and CD4-IgG [Moore1996]
- 15e: Anti-CD4BS MAbs 15e, 21h, and IgG1b12 did not cause gp120 dissociation from virus, or exposure of the gp41 epitope of MAb 50-69, in contrast to CD4i MAb 48d and anti-V3 neutralizing MAbs [Poignard1996a]
- 15e: Inhibits gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study [Trkola1996a]
- 15e: Neutralizes HIV-1 LAI less potently than V3 specific MAbs [McDougal1996]
- 15e: 15e is V H4 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals [Wisnewski1996]
- 15e: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric Env binding – 15e bound monomer, did not bind oligomer or neutralize JRFL [Fouts1997]
- 15e: One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB env – 15e could only achieve 50% neutralization, but could act synergistically with anti-V3 MAb 694/98-D to achieve 90% [Li1997]
- 15e: Does not bind to HXBc2 gp120 if the 19 C-term amino acids, in conjunction with C1 positions 31-93, are deleted [Wyatt1997]
- 15e: Called 1.5E – Binds to 7/7 isolates from breakthrough cases from a MN gp120 vaccine trial [Berman1997]
- 15e: Neutralizes TCLA strains, but not primary isolates [Parren1997c]
- 15e: Summary of the implications of the crystal structure of the core of gp120 bound to CD4 and 17b with what is known about mutations that reduce NAb binding – probable mechanism of neutralization by CD4BS Ab is direct interference with CD4 binding [Wyatt1998a]
- 15e: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren1998a]
- 15e: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer – CD4BS MAbs 15e, F91 and IgG1b12 bound better to the deleted protein than to wild type [Binley1998]
- 15e: Competes with CG-10 binding, a MAb raised against a gp120 CD4 complex, this was probably due to the disruption of CD4-gp120 by 15e [Sullivan1998b]
- 15e: No detectable neutralizing activity among primary isolates with different co-receptor usage – some neutralization of TCLA strains [Trkola1998]
- 15e: CD4BS MAbs 15e, 21h, and F91 bind with even lower affinity than 205-43-1 and 205-42-15 to JRFL oligomer [Fouts1998]
- 15e: Called 1.5e – the HIV-1 virus YU2 entry can be enhanced by MAbs binding to the CD4BS, V3 loop, and CD4i epitopes – the activation for this enhanced entry state could be conferred on HxB2 by introducing the YU2 V3 loop, or the YU2 V3 and V1/V2 loops – a similar effect is observed by sub-neutralizing concentrations of sCD4 and the effect is dependent of CCR5 – 1.5e enhances and does not neutralize YU2 env even at 50 ug/ml [Sullivan1998a]
- 15e: Six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20-100 fold more efficient at neutralizing the sensitive form – the mutation L544P reduced binding of all MAbs against gp120 by causing conformational changes [Park2000]
- 15e: Mutations in two glcosylation sites in the V2 region of HIV-1 ADA at positions 190 and 197 (187 DNTSYRLINCNTS 199) cause the virus to become CD4-independent and able to enter cells through CCR5 alone – these same mutations tended to increase the neutralization sensitivity of the virus, including to 15e [Kolchinsky2001]
- 15e: A series of mutational changes were introduced into the YU2 gp120 that favored different conformations – 375 S/W seems to favor a conformation of gp120 closer to the CD4-bound state, and is readily bound by sCD4 and CD4i MAbs (17b, 48d, 49e, 21c and 23e) but binding of anti-CD4BS MAbs (F105, 15e, IgG1b12, 21h and F91 was markedly reduced – IgG1b12 failed to neutralize this mutant, while neutralization by 2G12 was enhanced – 2F5 did not neutralize either WT or mutant, probably due to polymorphism in the YU2 epitope – another mutant, 423 I/P, disrupted the gp120 bridging sheet, favored a different conformation and did not bind CD4, CCR5, or CD4i antibodies, but did bind to CD4BS MAbs [Xiang2002b]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 15e: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain [Zhang2002] • 15e: Alanine scanning mutagenesis was used to compare substitutions that affected anti-CD4BS NAb b12 – rec gp120s were engineered to contain combinations of Alanine substitutions that enhanced b12 binding, and while binding of b12 to these gp120 monomers was generally maintained or increased, binding by five non-neutralizing anti-CD4bs MAbs (b3, b6, F105, 15e, and F91) was reduced or completely abolished [Pantophlet2003] • 15e: UK Medical Research Council AIDS reagent: ARP3016			
887	205-43-1	Env	gp120		no	HIV-1 infection	human
		Ab type CD4BS **References** Fouts1998, Grovit-Ferbas2000 • 205-43-1: Rank order of CD4BS antibodies oligomer binding is IgG1b12 = 2G6 = 205-46-9 > 205-43-1 = 205-42-15 > 15e = 21h = F91, and the only thing notably distinguishing about neutralizing IgG1b12 is that it depends on residues in V2 [Fouts1998] • 205-43-1: To determine the antigenicity of virus killed by thermal and chemical inactivation, retention of conformation-dependent neutralization epitopes was examined, and exposure of CD4BS epitopes was found to be enhanced (MAbs IgG1b12, 205-46-9, and 205-43-1) – binding to 2G12 and 447-52D epitopes was essentially unaltered – the 17b CD4i epitope was also exposed [Grovit-Ferbas2000]					
888	205-46-9	Env	gp120		no	HIV-1 infection	human
		Ab type CD4BS **References** Fouts1998, Grovit-Ferbas2000 • 205-46-9: Binds JRSF oligomer with high affinity as does IgG1b12, but IgG1b12 is neutralizing, 205-46-9 is not – conclusions of this paper contrast with Parren98 – authors propose a model where 205-46-9 and 2G6 may inhibit CD4 binding, but cause a conformational shift which enhances CCR5 binding and thus counteracts the neutralizing effect – rank order of CD4BS antibodies oligomer binding is IgG1b12 = 2G6 = 205-46-9 > 205-43-1 = 205-42-15 > 15e = 21h = F91, and the only thing notably distinguishing about neutralizing IgG1b12 is that it depends on residues in V2 [Fouts1998] • 205-46-9: To determine the antigenicity of virus killed by thermal and chemical inactivation, retention of conformation-dependent neutralization epitopes was examined, and exposure of CD4BS epitopes was found to be enhanced (MAbs IgG1b12, 205-46-9, and 205-43-1) – binding to 2G12 and 447-52D epitopes was essentially unaltered – the 17b CD4i epitope was also exposed [Grovit-Ferbas2000]					
889	21h (2.1H)	Env	gp120		L	HIV-1 infection	human (IgG1)
		Ab type CD4BS **Donor** James Robinson, Tulane University, LA **References** Ho1991b, Thali1992a, Ho1992, Wyatt1993, Moore1993a, Moore1994b, Moore1994a, Bagley1994, Thali1994, Sattentau1995b, Moore1996, Poignard1996a, Wisnewski1996, McKeating1996b, Binley1997a, Fouts1997, Li1997, Ugolini1997, Wyatt1997, Parren1997c, Wyatt1998a, Parren1998a, Fouts1998, Xiang2002b • 21h: Amino acid substitutions in HXB2 that inhibit binding, some shared with CD4 binding inhibition, 88, 113, 257, 368, 370, 421, 470, 480 [Thali1992a] • 21h: Binding to Delta V1/2 and Delta V1/2/3 mutant glycoproteins is greater than binding to wildtype gp120 [Wyatt1993] • 21h: Conformational, does not bind denatured gp120 – neutralizes IIIB – reactive with SF-2 gp120 – strong inhibition of HIV+ human sera binding to IIIB gp120 [Moore1993a] • 21h: Has strong cross-reactivity with gp120 monomers from most subtypes, A-F, with the least reactivity to clade E [Moore1994b] • 21h: Competition studies with human sera from seroconverting individuals showed that anti-CD4 BS antibodies can arise very early in infection, comparable or prior to anti-V3 antibodies [Moore1994a] • 21h: Heavy chain is V HIII, VDP-35 – light chain is V_lambdaIIIa, Hum318. Compared to 15e and F105 [Bagley1994]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 21h: A mutation in gp41, 582 A/T, confers resistance to neutralization (also confers resistance to MAbs F105, 48d, 15e and 17b) [Thali1994]
- 21h: Binds with higher affinity to monomer than to oligomer, moderate association rate [Sattentau1995b]
- 21h: Anti-CD4 binding site MAb – reciprocal inhibition by anti-C1, -C4 and other anti-CD4 binding site antibodies – enhanced by some anti-V2 MAbs and anti-V3 MAb 5G11 – enhances binding of some anti-V3 and -V2 MAbs [Moore1996]
- 21h: Anti-CD4BS MAbs 15e, 21h, and IgG1b12 did not cause gp120 dissociation from virus, or exposure of the gp41 epitope of MAb 50-69, in contrast to CD4i MAb 48d and anti-V3 neutralizing MAbs [Poignard1996a]
- 21h: 21h is V H3 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals [Wisnewski1996]
- 21h: Called 2.1H – Neutralizes HXB2, but fails to neutralize chimeric virus with gp120 from primary isolates in an HXB2 background [McKeating1996b]
- 21h: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric Env binding – 21h bound monomer, did not bind oligomer or neutralize JRFL [Fouts1997]
- 21h: One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB env – 50% neutralization could not be achieved at a maximal concentration of 67 mug/ml [Li1997]
- 21h: Viral binding inhibition by 21h strongly correlated with neutralization (all other neutralizing MAbs tested showed some correlation except 2F5) [Ugolini1997]
- 21h: Binds both gp120 and soluble gp120+gp41 complex efficiently, suggesting its gp120 epitope is not blocked by gp41 binding – major deletions in C1 and C5 and deletions of the V1V2 and V3 loops do not diminish binding [Wyatt1997]
- 21h: Neutralizes TCLA strains, but not primary isolates [Parren1997c]
- 21h: Summary of the implications of the crystal structure of the core of gp120 bound to CD4 and 17b with what is known about mutations that reduce NAb binding – probable mechanism of neutralization by CD4BS Ab is direct interference with CD4 binding [Wyatt1998a]
- 21h: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren1998a]
- 21h: CD4BS MAbs 15e, 21h, and F91 bind with even lower affinity than 205-43-1 and 205-42-15 to JRFL oligomer – conclusions of this paper contrast with [Parren1998a] [Fouts1998]
- 21h: A series of mutational changes were introduced into the YU2 gp120 that favored different conformations—375 S/W seems to favor a conformation of gp120 closer to the CD4-bound state, and is readily bound by sCD4 and CD4i MAbs (17b, 48d, 49e, 21c and 23e) but binding of anti-CD4BS MAbs (F105, 15e, IgG1b12, 21h and F91) was markedly reduced—IgG1b12 failed to neutralize this mutant, while neutralization by 2G12 was enhanced—2F5 did not neutralize either WT or mutant, probably due to polymorphism in the YU2 epitope—another mutant, 423 I/P, disrupted the gp120 bridging sheet, favored a different conformation and did not bind CD4, CCR5, or CD4i antibodies, but did bind to CD4BS MAbs [Xiang2002b].
- 21h: UK Medical Research Council AIDS reagent: ARP3017

890	28A11/B1	Env	gp120 (SF162)		L	Vaccine	human from transgenic mice (IgG2κ)

Vaccine *Vector/Type:* recombinant protein *Strain:* SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM)
Ab type CD4BS **Donor** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References He2002

- 28A11/B1: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—6 anti-CD4BS MAbs competed with anti-CD4BS MAb 5145A, blocked sCD4 binding and were conformationally sensitive—4/6 could neutralize the autologous strain SF162, and were broadly cross-reactive with B clade R5 and X4 strains (not E clade)—28A11/B1 was one of these four MAbs [He2002].

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
891	2G6	Env	gp120				

Ab type CD4BS **Donor** Herman Katinger, Inst. Appl. Microbiol. University of Agricultural Science, or Polymun Scientific Inc., Vienna, Austria
References Fouts1998

- 2G6: Binds to JRFL oligomer with an affinity comparable to IgG1b12, but does not neutralize the virus, so binding of oligomer is not always predictive of neutralization – conclusions of this paper contrast with [Parren1998a] – authors propose a model where 205-46-9 and 2G6 may inhibit CD4 binding, but cause a conformational shift which enhances CCR5 binding and thus counteracts the neutralizing effect [Fouts1998]

892	35F3/E2	Env	gp120 (SF162)		L	Vaccine	human from transgenic mice (IgG2κ)

Vaccine *Vector/Type:* recombinant protein *Strain:* SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM)
Ab type CD4BS **Donor** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References He2002

- 35F3/E2: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—6 anti-CD4BS MAbs competed with anti-CD4BS MAb 5145A, blocked sCD4 binding and were conformationally sensitive—4/6 could neutralize the autologous strain SF162, and were broadly cross-reactive with B clade R5 and X4 strains (not E clade)—35F3/E2 was one of these four MAbs [He2002].

893	38G3/A9	Env	gp120 (SF162)		L	Vaccine	human from transgenic mice (IgG2κ)

Vaccine *Vector/Type:* recombinant protein *Strain:* SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM)
Ab type CD4BS **Donor** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References He2002

- 38G3/A9: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—6 anti-CD4BS MAbs competed with anti-CD4BS MAb 5145A, blocked sCD4 binding and were conformationally sensitive—4/6 could neutralize the autologous strain SF162, and were broadly cross-reactive with B clade R5 and X4 strains (not E clade)—38G3/A9 was one of these four MAbs [He2002].

894	428	Env	gp120			HIV-1 infection	human

Ab type CD4BS
References Karwowska1992a, Jeffs1996

- 428: Slight, not significant increased binding when V1/V2 or V1/V2 and V3 were deleted from gp120 [Jeffs1996]

895	448-D (448D)	Env	gp120		L	HIV-1 infection	human (IgG1λ)

Ab type CD4BS **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU Med Center, NY, NY
References Karwowska1992a, McKeating1992c, Spear1993, Laal1994, Forthal1995, Manca1995a, Li1997, Wyatt1998a, Nyambi2000

- 448-D: Conformational – reactive with IIIB gp120 in RIP, but not WB assay [Karwowska1992a]
- 448-D: Called 448D – blocks gp120-CD4 binding – substitutions at gp120 residues 88, 113, 117, 257, 368 and 370 reduce binding – epitope similar to rat MAbs 39.13g and 39.3b [McKeating1992c]
- 448-D: Did not mediate deposition of complement component C3 on HIV infected cells [Spear1993]
- 448-D: Dissociation constant gp120 IIIB 0.029 – neutralizes IIIB, acts synergistically with anti-V3 MAb 447-52D [Laal1994]
- 448-D: Neutralizing activity, positive ADCC activity, and no viral enhancing activity [Forthal1995]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 448-D: Virions complexed to gp120 Ab facilitate presentation of p66 RT epitopes to Th cells [Manca1995a] • 448-D: One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB env [Li1997] • 448-D: Summary of the implications of the crystal structure of the core of gp120 bound to CD4 and 17b with what is known about mutations that reduce NAb binding – probable mechanism of neutralization by CD4BS Ab is direct interference with CD4 binding [Wyatt1998a] • 448-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 CD4BS MAbs – CD4BS MAbs bound consistently to most isolates of clade D, but poorly to isolates of other clades with the exception of broadly reactive MAb IgG1b12[Nyambi2000]				
896	44D2/D5	Env	gp120 (SF162)		no	Vaccine	human from transgenic mice (IgG2κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) **Ab type** CD4BS **Donor** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** He2002 • 44D2/D5: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—6 anti-CD4BS MAbs competed with anti-CD4BS MAb 5145A, blocked sCD4 binding and were conformationally sensitive—4/6 could neutralize the autologous strain SF162, and were broadly cross-reactive with B clade R5 and X4 strains (not E clade)—44D2/D5 could not neutralize autologous SF162, and while it was cross-reactive, it was at lower affinity [He2002].				
897	48-16	Env	gp120		no	HIV-1 infection	human (IgGκ)
		Ab type CD4BS **References** Fevrier1995 • 48-16: Broadly cross-reactive, reacts outside the CD4 binding site and V3 region—competes with sera from 45 seropositive subjects—binding affinity 2–5 $\times 10^{-9}$ M [Fevrier1995].					
898	50-61A	Env	gp120		L	HIV-1 infection	human (IgGκ)
		Ab type CD4BS **References** Fevrier1995 • 50-61A: Neutralizes lab strains LAI and SF2 – competes with sera from 45 seropositive subjects – binding affinity 2.4 x 10-10 M [Fevrier1995]					
899	5145A	Env	gp120		L	HIV-1 infection	human (IgG1)
		Ab type CD4BS **References** Pinter1993a, Warrier1996, Pincus1996, Alsmadi1998, He2002 • 5145A: Potent and broadly cross-reactive neutralization of lab strains [Pinter1993a] • 5145A: Synergistic neutralization of HIV-1 when combined with anti-V2 MAb C108G [Warrier1996] • 5145A: A panel of immunotoxins were generated by linking Env MAbs to ricin A – immunotoxins mediated cell killing, but killing was not directly proportional to binding [Pincus1996] • 5145A: A study of 6 anti-Env MAbs and their ability to bind or direct ADCC against target cells infected with IIIB, MN, SF-2, and RF – bound and directed lysis against all four strains [Alsmadi1998] • 5145A: Transgenic mice carrying human genes allowing production of fully human MAbs were used to rapidly create a panel of anti-HIV gp120 MAb producing hybridomas by immunization with HIV SF162 gp120 – the previously described human MAbs 5145A, 4117C and 697D were used as controls [He2002]				
900	558-D	Env	gp120		L	HIV-1 infection	human
		Ab type CD4BS **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU Med Center, NY, NY					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

References McKeating1992c, Nyambi1998

- 558-D: Blocks gp120-CD4 binding – binds a panel of mutants all except for 256 S/Y and 262 N/T, which are probably conformationally disruptive [McKeating1992c]
- 558-D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – CD4BS Abs tended to bind weakly without clade specificity to virions, but bound well to soluble gp120 – 558-D did not bind to any B clade viruses, and weakly bound to clade A, C, and G isolates – 559/64-D, 558-D and 1202-D had similar reactivities [Nyambi1998]

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901 559/64-D (559, 559-64D) Env gp120 (LAI) L HIV-1 infection human (IgG1κ)

Ab type CD4BS **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU Med Center, NY, NY

References Karwowska1992a, McKeating1992c, Spear1993, Stamatatos1995, Forthal1995, Jeffs1996, Hioe1997a, Hioe1997b, Nyambi1998, Gorny2000a, Hioe2000, Nyambi2000, Hioe2001, York2001

- 559/64-D: Conformational – reactive with IIIB gp120 in RIP, but not WB assay [Karwowska1992a]
- 559/64-D: Did not mediate deposition of complement component C3 on HIV infected cells [Spear1993]
- 559/64-D: Called 559-64D – The binding of conformation-dependent anti-V2, anti-V3, and anti-CD4BS MAbs to monomeric and virion-associated gp120 from HIV-1 isolates with differences in cell tropism was studied – CD4BS loop epitopes are somewhat occluded in the oligomeric gp120 epitopes on the virion surface relative to the gp120 monomer as indicated by an increase in the half-maximal binding values to macrophage-tropic isolates SF162 and SF128a and to T-cell tropic SF2 – binding of anti-CD4BS MAbs to SF2 resulted in a significant amount of dissociation of gp120 from virion surface [Stamatatos1995]
- 559/64-D: Neutralizing activity, no ADCC activity, and no viral enhancing activity [Forthal1995]
- 559/64-D: Called 559 – slight, not significant increased binding when V1/V2 or V1/V2 and V3 were deleted from gp120 [Jeffs1996]
- 559/64-D: Used in the development of resting cell neutralization assay [Hioe1997a]
- 559/64-D: Four primary isolates showed distinct patterns of sensitivity to neutralization by polyclonal sera or plasma and MAbs – BZ167 was the only isolate inhibited by all polyclonal sera and plasma tested, and was also neutralized by 8/17 MAbs, in particular anti-V3 loop (419-D, 447-52D, 782-D, and 838-D), anti-CD4bd (559/64-D, 654-D and 830-D and a cluster II of gp41 directed MAb (98-6) – isolates 92HT593 and 91US056 were neutralized by V3 loop (419-D, and 447-52D)and cluster II gp41 (98-6) MAbs at higher concentrations – US4 was neutralized by some of the polyclonal sera/plasma tested and not at all by MAbs individually or by a cocktail of ten MAbs consisting of 419-D, 447-52D, 782-D, 838-D, 559/64-D, 654-D, 450-D, 670-D, 1281-D and 98-6 [Hioe1997b]
- 559/64-D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – CD4BS Abs tended to bind weakly without clade specificity to virions, but bound well to soluble gp120 – 559/64-D did not bind to any B clade viruses, and weakly bound clade A, C, and G isolates – 559/64-D, 558-D and 1202-D had similar reactivities [Nyambi1998]
- 559/64-D: Binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – CD4BS MAbs 559/64-D, 654-D, 729-D, 9CL and 1331E bound with a 5-13 fold preference for the oligomer [Gorny2000a]
- 559/64-D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – anti-CD4 binding site MAbs or serum Ig from HIV+ individuals inhibited proliferative responses of gp120 specific T cells – CD4BS MAbs 654-D, 559/64-D, 588-D, 830-D, 1027-30-D, and 1202-30D strongly diminished proliferation [Hioe2000]
- 559/64-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 CD4BS MAbs – CD4BS MAbs bound consistently to most isolates of clade D, but poorly to isolates of other clades with the exception of broadly reactive MAb IgG1b12[Nyambi2000]
- 559/64-D: CD4BS MAbs when complexed with gp120, inhibit proliferation of gp120-specific CD4 T-cells and IFNγ production—anti-CD4BS MAbs inhibit gp120 presentation by altering the uptake and/or processing of gp120 by the APCs, not by blocking of gp120 attachment to CD4 on the surface of APCs [Hioe2001].

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 559/64-D: Abs against the V3 loop (50.1, 58.2, 59.1, 257-D, 268-D, 447-52D), CD4BS (IgG1b12, 559-64D, F105), CD4 induced or CD4i (17b), and to gp41 (2F5, F240) each showed similar binding efficiency to Env derived from related pairs of primary and TCLA lines (primary: 168P and 320SI, and TCLA: 168C and 320SI-C3.3), but the TCLA lines were much more susceptible to neutralization suggesting that the change in TCLA lines that make them more susceptible to NAbs alters some step after binding [York2001]					
902	55D5/F9	Env	gp120 (SF162)		L	Vaccine	human from transgenic mice (IgG2κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) **Ab type** CD4BS **Donor** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** He2002 • 55D5/F9: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—6 anti-CD4BS MAbs competed with anti-CD4BS MAb 5145A, blocked sCD4 binding and were conformationally sensitive—4/6 could neutralize the autologous strain SF162, and were broadly cross-reactive with B clade R5 and X4 strains (not E clade)—55D5/F9 was one of these four MAbs [He2002].					
903	588-D (588)	Env	gp120		L	HIV-1 infection	human (IgG1κ)
		Ab type CD4BS **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU Med Center, NY, NY **References** Karwowska1992a, Buchbinder1992, Moore1993a, Jeffs1996, Nyambi1998, Hioe2000, Nyambi2000 • 588-D: Conformational – reactive with IIIB gp120 in RIP, but not WB assay [Karwowska1992a] • 588-D: 4-fold increase in neutralization potency for 588-D when combined 1:1 with human MAb 447-D [Buchbinder1992] • 588-D: Weak neutralization of IIIB – strong inhibition of HIV+ human sera binding to IIIB gp120 [Moore1993a] • 588-D: Called 588 – slight, not significant increased binding when V1/V2 or V1/V2 and V3 were deleted from gp120 [Jeffs1996] • 588-D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – CD4-BS Abs tended to bind weakly without clade specificity to virions, but bound well to soluble gp120 – 588-D did not bind to any B clade viruses, and weakly bound a clade A, C, and G clade isolate – 559/64-D, 558-D and 1202-D reacted had similar reactivities [Nyambi1998] • 588-D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – anti-CD4 binding site MAbs or serum Ig from HIV+ individuals inhibited proliferative responses of gp120 specific T cells – CD4BS MAbs 654-D, 559/64-D, 588-D, 830-D, 1027-30-D, and 1202-30D strongly diminished proliferation [Hioe2000] • 588-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 CD4BS MAbs – CD4BS MAbs bound consistently to most isolates of clade D, but poorly to isolates of other clades with the exception of broadly reactive MAb IgG1b12[Nyambi2000]					
904	654-D (654-30D, 654/30D, 654-D100, 654.30D, 654)	Env	gp120 (LAI)		L	HIV-1 infection	human (IgGκ)
		Ab type CD4BS **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU Med Center, NY, NY **References** Karwowska1993, Laal1994, Gorny1994, Stamatatos1995, Li1997, Stamatatos1997, Gorny1997, Hioe1997b, Gorny1998, Schonning1998, Nyambi1998, Stamatatos1998, Hioe1999, Gorny2000a, Hioe2000, Hioe2001, Nyambi2000, Verrier2001, Gorny2002 • 654-D: Dissociation constant gp120 IIIB 0.008 – neutralizes IIIB, acts synergistically with anti-V3 MAb 447-52D – reported to be human(IgG1lambda) [Laal1994] • 654-D: Mild oxidation of carbohydrate moieties inhibits binding [Gorny1994]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 654-D: Called 654-30D – The binding of conformation-dependent anti-V2, anti-V3, and anti-CD4BS MAbs to monomeric and virion-associated gp120 from HIV-1 isolates with differences in cell tropism was studied – CD4BS loop epitopes are somewhat occluded in the oligomeric gp120 epitopes on the virion surface relative to the gp120 monomer as indicated by an increase in the half-maximal binding values to macrophage-tropic isolates SF162 and SF128a and to T-cell tropic SF2 – binding of anti-CD4BS MAbs to SF2 resulted in a significant amount of dissociation of gp120 from virion surface [Stamatatos1995]
- 654-D: Called 654-30D – One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB env [Li1997]
- 654-D: Anti-CD4 BS MAb 654-30D and IgG1b12 have comparable binding affinities, neither mediates gp120-virion dissociation, but IgG1b12 can neutralize SF128A and SF162 and 654-D cannot – 654-D actually enhances infection by both viruses in primary macrophages [Stamatatos1997]
- 654-D: Four primary isolates showed distinct patterns of sensitivity to neutralization by polyclonal sera or plasma and MAbs – BZ167 was the only isolate inhibited by all polyclonal sera and plasma tested, and was also neutralized by 8/17 MAbs, in particular anti-V3 loop (419-D, 447-52D, 782-D, and 838-D), anti-CD4bd (559/64-D, 654-D and 830-D and a cluster II of gp41 directed MAb (98-6) – isolates 92HT593 and 91US056 were neutralized by V3 loop (419-D, and 447-52D)and cluster II gp41 (98-6) MAbs at higher concentrations – US4 was neutralized by some of the polyclonal sera/plasma tested and not at all by MAbs individually or by a cocktail of ten MAbs consisting of 419-D, 447-52D, 782-D, 838-D, 559/64-D, 654-D, 450-D, 670-D, 1281-D and 98-6 [Hioe1997b]
- 654-D: Called 654-D100 – 654-D100 and IgG1b12 neutralized viruses HIV-BRU and a mutated virus that lacks the V3 loop glycan equally effectively – in contrast, sera from guinea pigs immunized with BRU gp120 neutralize viruses more effectively that lack the V3 glycan[Schonning1998]
- 654-D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – CD4-BS Abs tended to bind very weakly without clade specificity to virions, but bound well to soluble gp120 – 654-D bound only to JRFL [Nyambi1998]
- 654-D: Called 654.30D – deleting the V2 loop of neutralization-resistant HIV-1 isolate SF162 does not abrogate its replication in PBMC or macrophages, but it enhances its neutralization sensitivity to sera from patients with B clade infection up to 170-fold, and also enhances sensitivity to sera from clades A through F – deletion of V2 but not V1 slightly allowed neutralization by CD4BS MAb 654.30D [Stamatatos1998]
- 654-D: The presence of leukocyte function-associated molecule 1 (LFA-1) promotes virus infectivity and hinders neutralization, and anti-LFA-1 MAbs can enhance the neutralizing effect of anti-HIV V3 MAb 447-52D and anti-HIV CD4BS MAb IgG1b12 – non-neutralizing anti-HIV CD4BS MAb 654-D did not become neutralizing in the presence of anti-LFA-1 MAbs [Hioe1999]
- 654-D: Binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – CD4BS MAbs 559/64-D, 654-D, 729-D, 9CL and 1331E bound with a 5-13 fold preference for the oligomer [Gorny2000a]
- 654-D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – CD4BS MAbs or serum Ig from HIV+ individuals inhibited proliferative responses of gp120 specific T cells – MAb 654-D strongly diminished proliferation – there is a discrepancy in isotyping this antibody, previous reports indicated IgG1kappa, while Hioe suggests it is IgG1lambda [Hioe2000]
- 654-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 CD4BS MAbs – CD4BS MAbs bound consistently to most isolates of clade D, but poorly to isolates of other clades with the exception of broadly reactive MAb IgG1b12 – 654-D had the weakest binding among CD4BS MAbs, binding to only 4/26 isolates [Nyambi2000]
- 654-D: CD4BS MAbs when complexed with gp120, inhibit proliferation of gp120-specific CD4 T-cells and IFN gamma production – anti-CD4BS MAbs inhibit gp120 presentation by altering the uptake and/or processing of gp120 by the APCs, not by blocking of gp120 attachment to CD4 on the surface of APCs [Hioe2001]
- 654-D: A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6—six gave significant neutralization at 2 to 10 ug/ml: 2F5, 50-69, IgG1b12, 447-52D, 2G12, and 670-D, while six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98-6, and 1281—no synergy, only additive effects were seen for pairwise combinations of MAbs, and antagonism was noted between gp41 MAbs 50-69 and 98-6, as well as 98-6 and 2F5 [Verrier2001].

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 654-D: Called 654: Conformation-dependent anti-V3 loop Abs may be more cross-reactive, so six new V3 MAbs were generated – the six new MAbs all bind to the tip of the V3 loop and cross-compete with the MAb 447-52D and are conformationally sensitive – MAbs showed cross-clade binding to native, intact virions and the strength binding was highly correlated with percent neutralization using the ghost cell or PHA blast assay – five well-characterized MAbs were used as controls: anti-V3 447-52D (anti-V3 MAb for competition and neutralization studies), 654 (anti-CD4BS used as a conformation-sensitive MAb control), 1331A (anti-C5 used as a linear binding site MAb control), and MAb 246 (anti-gp41 MAb that bound to primary isolates of all clades) [Gorny2002]					
905	67G6/C4	Env	gp120 (SF162)		no	Vaccine	human from transgenic mice (IgG2κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) **Ab type** CD4BS **Donor** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** He2002 • 67G6/C4: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—6 anti-CD4BS MAbs competed with anti-CD4BS MAb 5145A, blocked sCD4 binding and were conformationally sensitive—4/6 could neutralize the autologous strain SF162, and were broadly cross-reactive with B clade R5 and X4 strains (not E clade)—67G6/C4 could not neutralize autologous SF162, and its binding was strain-specific [He2002].					
906	729-D (729-30D)	Env	gp120 (LAI)		L	HIV-1 infection	human (IgG1κ)
		Ab type CD4BS **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU Med Center, NY, NY **References** Laal1994, D'Souza1997, Li1997, Parren1997c, Gorny2000a • 729-D: Dissociation constant gp120 IIIB 0.025 – neutralizes IIIB, acts synergistically with anti-V3 MAb 447-52D [Laal1994] • 729-D: In a multilaboratory blinded study, failed to consistently neutralize any of nine B clade primary isolates – reported here to have a lambda light chain, but originally reported in [Laal1994] to be IgG1kappa [D'Souza1997] • 729-D: Called 720-30D – one of 14 human MAbs tested for ability to neutralize chimeric SHIV-vpu+, which expressed HIV-1 IIIB env [Li1997] • 729-D: Neutralizes TCLA strains, but not primary isolates [Parren1997c] • 729-D: Binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – CD4BS MAbs 559/64-D, 654-D, 729-D, 9CL and 1331E bound with a 5-13 fold preference for the oligomer [Gorny2000a]					
907	830D (830-D)	Env	gp120		L		human (IgG1κ)
		Ab type CD4BS **References** Hioe1997b, Wyatt1998a, Hioe2000 • 830D: Called 830-D: Four primary isolates showed distinct patterns of sensitivity to neutralization by polyclonal sera or plasma and MAbs – BZ167 was the only isolate inhibited by all polyclonal sera and plasma tested, and was also neutralized by 8/17 MAbs, in particular anti-V3 loop (419-D, 447-52D, 782-D, and 838-D), anti-CD4bd (559/64-D, 654-D and 830-D and a cluster II of gp41 directed MAb (98-6) – isolates 92HT593 and 91US056 were neutralized by V3 loop (419-D, and 447-52D)and cluster II gp41 (98-6) MAbs at higher concentrations – US4 was neutralized by some of the polyclonal sera/plasma tested and not at all by MAbs individually or by a cocktail of ten MAbs consisting of 419-D, 447-52D, 782-D, 838-D, 559/64-D, 654-D, 450-D, 670-D, 1281-D and 98-6 [Hioe1997b] • 830D: Summary of the implications of the crystal structure of the core of gp120 bound to CD4 and 17b with what is known about mutations that reduce NAb binding – probable mechanism of neutralization by CD4BS Ab is direct interference with CD4 binding [Wyatt1998a]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 830D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – anti-CD4 binding site MAbs or serum Ig from HIV+ individuals inhibited proliferative responses of gp120 specific T cells – CD4BS MAbs 654-D, 559/64-D, 588-D, 830-D, 1027-30-D, and 1202-30D strongly diminished proliferation [Hioe2000]					
908	9CL	Env	gp120 (LAI)			HIV-1 infection	human
		Ab type CD4BS **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU Med Center, NY, NY **References** Gorny2000a					
		• 9CL: Binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – CD4BS MAbs 559/64-D, 654-D, 729-D, 9CL and 1331E bound with a 5-13 fold preference for the oligomer [Gorny2000a]					
909	BM12	Env	gp120		L	HIV-1 infection	human
		Ab type CD4BS **References** Kessler1995					
		• BM12: Broad cross-clade neutralization of primary isolates – additive effect in combination with MAb 2F5 [Kessler1995]					
910	D20	Env	gp120 (IIIB)		no	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140 **Ab type** CD4BS **Donor** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD **References** Earl1994, Broder1994, Richardson1996, Otteken1996, Earl1997, Sugiura1999					
		• D20: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response [Earl1994] • D20: Binding completely blocked by pooled human sera [Broder1994] • D20: Human sera blocked binding in oligomeric ELISA assay to a similar extent for gp41 MAbs D20, D43, D61, and T4 [Richardson1996] • D20: Pulse label experiments of 4 MAbs (D20, D27, T20, and T22) binding to noncleavable gp160 revealed that these anti-CD4 MAbs bound with a delay, and that the epitope formed with a t 1/2 of about 10 minutes [Otteken1996] • D20: Used for comparison in a study of gp41 antibodies – D20 binds to a greater extent to cell surface expressed Env than any of 38 conformation dependent anti-gp41 MAbs [Earl1997] • D20: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D20 is part of a group of MAbs labeled A1 – all A1 MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, blocked CD4 binding, were sensitive to mutations in gp120 positions 368 and 370 that directly contact CD4 [Sugiura1999]					
911	D21	Env	gp120 (IIIB)			Vaccine	murine (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140 **Ab type** CD4BS **Donor** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD **References** Earl1994, Sugiura1999					
		• D21: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response [Earl1994] • D21: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D21 is part of a group of MAbs labeled A1 – all A1 MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, blocked CD4 binding, were sensitive to mutations in gp120 positions 368 and 370 that directly contact CD4 [Sugiura1999]					
912	D24	Env	gp120 (IIIB)		no	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140 **Ab type** CD4BS **Donor** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD **References** Earl1994, Sugiura1999					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• D24: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response [Earl1994] • D24: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D24 is part of a group of MAbs labeled B-I, that had limited cross-reactivity – of seven clade B isolates BH8 and B-al were they only two that consistently reacted with B-I MAbs – B-I MAbs fully blocked CD4 binding [Sugiura1999]					
913	D25	Env	gp120 (IIIB)			Vaccine	murine (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140 **Ab type** CD4BS **Donor** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD **References** Earl1994, Sugiura1999 • D25: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response [Earl1994] • D25: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D25 is part of a group of MAbs labeled A1 – all A1 MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, blocked CD4 binding, were sensitive to mutations in gp120 positions 368 and 370 that directly contact CD4 [Sugiura1999]					
914	D28	Env	gp120 (IIIB)		no	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140 **Ab type** CD4BS **Donor** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD **References** Earl1994, Sugiura1999 • D28: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response [Earl1994] • D28: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D28 is part of a group of MAbs labeled B-I, that had limited cross-reactivity – of seven clade B isolates BH8 and B-al were they only two that consistently reacted with B-I MAbs – B-I MAbs fully blocked CD4 binding [Sugiura1999]					
915	D35	Env	gp120 (IIIB)			Vaccine	murine (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140 **Ab type** CD4BS **Donor** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD **References** Earl1994, Sugiura1999 • D35: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response [Earl1994] • D35: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D35 is part of a group of MAbs labeled B-I, that had limited cross-reactivity – of seven clade B isolates BH8 and B-al were they only two that consistently reacted with B-I MAbs – B-I MAbs fully blocked CD4 binding [Sugiura1999]					
916	D39	Env	gp120 (IIIB)			Vaccine	murine (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140 **Ab type** CD4BS **Donor** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD **References** Earl1994, Sugiura1999 • D39: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response [Earl1994] • D39: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D39 is part of a group of MAbs labeled A1 – all A1 MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, blocked CD4 binding, were sensitive to mutations in gp120 positions 368 and 370 that directly contact CD4 [Sugiura1999]					
917	D42	Env	gp120 (IIIB)			Vaccine	murine (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140 **Ab type** CD4BS **Donor** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Earl1994, Sugiura1999 • D42: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response [Earl1994] • D42: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D42 is part of a group of MAbs labeled B-I, that had limited cross-reactivity – of seven clade B isolates BH8 and B-al were they only two that consistently reacted with B-I MAbs – B-I MAbs fully blocked CD4 binding [Sugiura1999]					
918	D52	Env	gp120 (IIIB)			Vaccine	murine (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140 **Ab type** CD4BS **Donor** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD **References** Earl1994, Sugiura1999 • D52: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response [Earl1994] • D52: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D52 is part of a group of MAbs labeled B-I, that had limited cross-reactivity – of seven clade B isolates BH8 and B-al were they only two that consistently reacted with B-I MAbs – B-I MAbs fully blocked CD4 binding [Sugiura1999]					
919	D53	Env	gp120 (IIIB)			Vaccine	murine (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140 **Ab type** CD4BS **Donor** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD **References** Earl1994, Sugiura1999 • D53: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response [Earl1994] • D53: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D53 is part of a group of MAbs labeled B-I, that had limited cross-reactivity – of seven clade B isolates BH8 and B-al were they only two that consistently reacted with B-I MAbs – B-I MAbs fully blocked CD4 binding [Sugiura1999]					
920	D60	Env	gp120 (IIIB)		no	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140 **Ab type** CD4BS **Donor** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD **References** Earl1994, Richardson1996, Sugiura1999 • D60: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response [Earl1994] • D60: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D60 is part of a group of MAbs labeled B-I, that had limited cross-reactivity – of seven clade B isolates BH8 and B-al were they only two that consistently reacted with B-I MAbs – B-I MAbs fully blocked CD4 binding [Sugiura1999]					
921	DA48	Env	gp120 (BRU)			HIV-1 infection	human
		Ab type CD4BS **References** Parren1998a, Sullivan1998a • DA48: The rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142-10 > DA48 > L17) was markedly different than Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142-10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren1998a]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- DA48: The HIV-1 virus YU2 entry can be enhanced by MAbs binding to the CD4BS, V3 loop, and CD4i epitopes – the activation for this enhanced entry state could be conferred on HxB2 by introducing the YU2 V3 loop, or the YU2 V3 and V1/V2 loops – a similar effect is observed by sub-neutralizing concentrations of sCD4 and the effect is dependent of CCR5 – Fab Ab fragment DA48 also enhances YU2 entry, ruling out Fc interactions or Env cross-linking as a mechanism – while DA48 enhances YU2, it neutralizes HXBc2 – DA48 was obtained by panning libraries derived from bone marrow from a >15 year long term non-progressor against BRU gp120 [Sullivan1998a]

922 DO8i Env gp120 (BRU) HIV-1 infection human Fab

Ab type CD4BS

References Parren1998a

- DO8i: The rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142-10 > DA48 > L17) was markedly different than Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142-10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren1998a]
- DO8i – the HIV-1 virus YU2 entry can be enhanced by MAbs binding to the CD4BS, V3 loop, and CD4i epitopes – the activation for this enhanced entry state could be conferred on HxB2 by introducing the YU2 V3 loop, or the YU2 V3 and V1/V2 loops – a similar effect is observed by sub-neutralizing concentrations of sCD4 and the effect is dependent of CCR5 – Fab fragment DO8i also enhances YU2 entry, ruling out Fc interactions or Env cross-linking as a mechanism, while neutralizing HXBc2 – DO8i was obtained by panning libraries derived from bone marrow from a long term asymptomatic donor against BRU gp120 [Sullivan1998a]

923 F105 (F-105) Env gp120 L HIV-1 infection human (IgG1κ)

Ab type CD4BS **Donor** Marshall Posner, Boston MA

References Posner1991, Thali1991, Thali1992a, Marasco1992, Wyatt1992, Posner1992b, Posner1992a, Moore1993a, Posner1993, Cavacini1993a, Cavacini1993b, Wyatt1993, Montefiori1993, Potts1993, Klasse1993a, Pincus1993b, Watkins1993, Marasco1993, Bagley1994, Thali1994, Cook1994, Cavacini1994b, Cavacini1994a, Earl1994, Chen1994a, Turbica1995, Posner1995, Cavacini1995, Sullivan1995, Khouri1995, Jagodzinski1996, Wolfe1996, McDougal1996, Wisnewski1996, Pincus1996, Litwin1996, Chen1996, Parren1997c, D'Souza1997, Li1997, Cao1997b, Wyatt1997, Wyatt1998a, Cavacini1998b, Li1998, Cavacini1998a, Brand1998, Sullivan1998a, Kropelin1998, Sugiura1999, Giraud1999, Cavacini1999, Oscherwitz1999a, Robert-Guroff2000, Baba2000, Park2000, Yang2000, Si2001, Kolchinsky2001, York2001, Yang2002, Xu2002, Chakrabarti2002, Xiang2002b, Edwards2002, Grundner2002, Basmaciogullari2002, Zhang2002, Ferrantelli2002, Liu2002, Pantophlet2003

- F105: First description of F105, binds topographically near the CD4-binding site – inhibits binding of free, infectious virions to uninfected HT-H9 cells, but does not react with virus adsorbed to uninfected HT-H9 cells – soluble rCD4 pre-bound to infected cells inhibits F105 binding – F105 inhibits infection of HT-H9 cells in standard neutralization assays with HIV-1 and MN strains [Posner1991]
- F105: F105 neutralization escape mutants result from changes in amino acids in discontinuous regions: C2, 256-262 and C3, 386-370 [Thali1991]
- F105: Amino acid substitutions that impair F105 neutralization inhibit gp120-CD4 interaction [Thali1992a]
- F105: MAb cDNA sequence – V H4 V71-4 rearranged with a D H D-D fusion product of dlr4 and da4, and with J H5 – V kappa is from the Humvk325 germline gene joined with Jkappa 2 [Marasco1992]
- F105: Precipitation of Delta 297-329 env glycoprotein, which has a deleted V3 loop, is much more efficient than precipitation of wild type [Wyatt1992]
- F105: F105 mediates ADCC against SF2 through the CD16+ population of PBMC – does not mediate complement-dependent cytotoxicity [Posner1992b]
- F105: Significant enhancement of F105 binding to RF infected cells preincubated with V3-specific MAbs V3-2 and V3-1 [Posner1992a]
- F105: Called F-105 – neutralizes IIIB – strong inhibition of HIV+ human sera binding to IIIB gp120 [Moore1993a]
- F105: F105 binds to and neutralizes selected lab strains and 3/9 HIV-1 primary isolates – synergistic enhancement of neutralization by seropositive sera [Posner1993]
- F105: No neutralization of primary isolates observed (John Moore, pers comm)
- F105: Additive MN or SF2 neutralization when combined with anti-V3 MAbs 447-52D and 257-D [Cavacini1993a]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- F105: Serum from all asymptomatic HIV-1 positive people tested block F105 binding, but only from 27% of symptomatic individuals [Cavacini1993b]
- F105: Binding to Delta V1/2 and Delta V1/2/3 mutant glycoproteins is 2.4- and 13-fold greater, respectively, than binding to wildtype gp120 [Wyatt1993]
- F105: Study of synergism between F105 and sera from vaccinated volunteers with V3-loop specific neutralization activity – 2/3 sera demonstrated neutralization synergy, and 3/3 binding/fusion-inhibition synergy [Montefiori1993]
- F105: Study of synergism of neutralization and binding comparing F105 and sCD4 with the V3 MAbs: 50.1, 59.1, 83.1, and 58.2 – synergy was observed, and the data suggest that binding of one ligand (F105) can increase the binding of the second (e. g. V3 loop MAbs) due to conformational changes [Potts1993]
- F105: The gp41 mutation 582(Ala to Thr) results in conformational changes in gp120 that confer neutralization resistance to a class of conformation sensitive neutralizing MAbs – required >81 fold higher concentrations to neutralize the mutant than wild type [Klasse1993a]
- F105: Ab response in IIIB lab workers was compared to gp160 LAI vaccine recipients – F105 was used as a control – infected lab workers and some of the gp160 vaccinees had a MAb response that could inhibit gp120-CD4 binding, at lower titers than the infected lab workers [Pincus1993b]
- F105: A neutralization escape mutant (HXB2 A281V) was selected by growth of HXB2 in the presence of broadly neutralizing sera – F105 neutralization was not affected by this mutation [Watkins1993]
- F105: Comparison of MAb F105 sequences with those of MAbs 21h and 15e [Bagley1994]
- F105: A mutation in gp41, 582 A/T, confers resistance to neutralization (also confers resistance to MAbs 48d, 21h, 15e and 17b) [Thali1994]
- F105: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – anti-CD4 MAbs moderately inhibit gp120 binding to GalCer, possibly through steric hindrance – binding of GalCer to gp120 inhibited but did not completely block F105 binding[Cook1994]
- F105: Administered intravenously to four cynomologus monkeys, plasma pharmacokinetics and biological activity tested [Cavacini1994b]
- F105: Fab fragments show reduced capacity to neutralize IIIB, MN, and RF compared to intact IgG1, suggesting bivalent interaction may be important in binding and neutralization [Cavacini1994a]
- F105: Used as a positive control for CD4 BS antibodies in a study of the influence of oligomeric structure of Env in determining the repertoire of the Ab response [Earl1994]
- F105: A human CD4+ T lymphocyte line was transduced to express Fab fragments of F105 – heavy and light chains are joined by an inter-chain linker – in the transduced cells infected with HIV-1, the Fab binds intracellularly to the envelope protein and inhibits HIV-1 production – secreted Fab fragments neutralize cell-free HIV-1 – combined intra- and extracellular binding activities of the expressed Fab make transduced cells resistant to HIV-1 infection and also can protect surrounding lymphocytes by secreting neutralizing antibodies [Marasco1993, Chen1994a]
- F105: An immunoassay for titrating CD4BS serum antibody was developed using a gp120-coated solid phase and competition with MAb F105 – 109/110 French HIV-1+ sera and 51/56 HIV-1+ African sera had detectable CD4BS Abs using this assay, demonstrating CD4 binding site conservation among diverse subtypes – CD4BS Abs were detected soon after seroconversion and persisted – 0/21 HIV-2+ sera reacted, indicating that the HIV-1 and HIV-2 CD4BS Abs are not cross-reactive [Turbica1995]
- F105: Eight patient phase Ia trial for use as an immunotherapeutic – no clinical or biochemical side effects observed, plasma levels of 10 ug/ml maintained for 21 days [Posner1995]
- F105: Efficient neutralization of T-cell adapted lines HXBc2 and MN, no neutralization of primary isolates 89.6, ADA and YU2 – even some enhancement of infection of ADA and YU2 was observed [Sullivan1995]
- F105: Biotinylated F105 was used for competition studies with Ab derived from pregnant HIV-1+ women – a correlation between maternal anti-CD4 BS Abs overlapping the F105 binding site and lack of HIV-1 transmission to infants was noted [Khouri1995]
- F105: Changing heavy chain from IgG1 to IgG3 increased neutralization efficiency [Cavacini1995]
- F105: The sulfated polysaccharide curdlan sulfate (CRDS) binds to the Envelope of T-tropic viruses and neutralizes virus – deletion of the V3 loop results in less potent inhibition of F105 binding by CRDS – binding site of F105 described as 256-257 ST, 368-370 DPE, 421 K, and 470-484 PGGGDMRDNWRSELY [Jagodzinski1996]
- F105: Phase I study – MAb clearance in plasma has a 13 day half-life [Wolfe1996]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- F105: Neutralizes HIV-1 LAI less potently than V3 specific MAbs [McDougal1996]
- F105: F105 is V H4 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals [Wisnewski1996]
- F105: A panel of immunotoxins were generated by linking Env MAbs to ricin A – immunotoxins mediated cell killing, but killing was not directly proportional to binding [Pincus1996]
- F105: Binding of F105 to oligomeric gp120 occurs despite the fact it cannot neutralize primary isolates [Litwin1996]
- F105: Intracellular co-expression of heavy and light chains of the Fab105 fragment MAb F105 was enhanced by inclusion of an internal ribosome entry site (IRES) sequence – the Fab105 IRES expression cassette was cloned into an adeno-associated virus (AAV) shuttle vector, and transduced into human lymphocytes which were able to produce and secrete the Fab105 fragments while maintaining normal growth – several primary HIV-1 patient isolates were effectively blocked [Chen1996]
- F105: Neutralizes TCLA strains, but not primary isolates [Parren1997c]
- F105: In a multilaboratory blinded study, failed to neutralize any of nine B clade primary isolates [D'Souza1997]
- F105: One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB env – F105 could only achieve 50% neutralization alone – all Ab combinations tested showed synergistic neutralization – F105 has synergistic response with MAbs 694/98-D (anti-V3), 48d, 2F5, and 2G12, and also with HIVIG [Li1997]
- F105: Virus with the V1-V2 loop deleted was viable and more susceptible to neutralization by CD4i MAb 17b, and anti-V3 MAbs 1121, 9284, and 110.4, but not to a CD4BS MAb, F105 or sCD4 [Cao1997b]
- F105: Binds both gp120 and soluble gp120+gp41 complex efficiently, suggesting its gp120 epitope is not blocked by gp41 binding – does not bind to HXBc2 gp120 if the 19 C-term amino acids, in conjunction with C1 positions 31-93, are deleted [Wyatt1997]
- F105: Summary of the implications of the crystal structure of the core of gp120 bound to CD4 and 17b with what is known about mutations that reduce NAb binding – probable mechanism of neutralization by CD4BS Ab is direct interference with CD4 binding [Wyatt1998a]
- F105: Phase I dose escalation study, single dose of 100 or 500 mg/m2 was given to 4 HIV+ patients – sustained levels, no immune response against F105, no toxicity, infused Ab retained function – there was no evidence of anti-HIV-1 activity and virus was not diminished at day 1 or 7, by culture or plasma RNA [Cavacini1998b]
- F105: Neutralization synergy was observed when the MAbs 694/98-D (V3), 2F5 (gp41), and 2G12 (gp120 discontinuous) were used in combination, and even greater neutralizing potential was seen with the addition of a fourth MAb, F105 (CD4 BS) [Li1998]
- F105: The MAb F240 binds to the immunodominant region of gp41 and enhances infection in the presence of complement – reactivity of F240 is enhanced by preincubation of cells with sCD4 or anti-CD4BS MAb F105 [Cavacini1998a]
- F105: Immunoprecipitation of gp120 and gp160 expressed from a rec Semliki Forest virus by F105 and IgG1b12 indicated that the SFV expressed HIV-1 Env was folded appropriately – and SVF-HIV-1 Env vaccine gave the strongest anti-HIV-1 Env response in mice, when compared to an HIV-1 Env DNA vaccine and a rgp160 protein [Brand1998]
- F105: A comparison of 25 gp120 specific, conformation dependent MAbs was done and F105 was used for competition studies – F105 did cross-compete with multiple CD4BS specific MAbs, however most could not neutralize even the autologous NL4-3 strains [Sugiura1999]
- F105: F105 enhances viral entry of viruses carrying the YU2 envelope glycoproteins, but neutralizes HXBc2 [Sullivan1998a]
- F105: Anti-C1 region MAb 87-135/9 blocks gp120 interaction with CD4+ cells – blocking activity is additive when combined with antibodies which bind in the C4 region of gp120 (F105, 388/389, and b12) [Kropelin1998]
- F105: A mini-review of observations of passive administration of IgG NAbs conferring protection against intervenous or vaginal SHIV challenge, that considers why IgG MAbs might protect against mucosal challenge [Robert-Guroff2000]
- F105: A triple combination of 2F5, F105 and 2G12 effectively neutralized perinatal infection of macaque infants when challenged with SHIV-vpu+ – the plasma half-life was 7.2 +/- 2.2 days [Baba2000]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- F105: Host encoded intercellular adhesion molecule (ICAM-1) is incorporated by the HIV-1 virion and enhances viral infectivity – ICAM-1 does not modify virus sensitivity to antibodies 0.5beta or 4.8D or sCD4, but neutralizing ability of F105 was diminished in ICAM bearing virions in the presence of lymphocyte function-association antigen-1 (LFA-1) Ab [Fortin2000]
- F105: Six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20-100 fold more efficient at neutralizing the sensitive form, although F105 was an exception and cannot neutralize either form of MN – the mutation L544P reduced binding of all MAbs against gp120 by causing conformational changes [Park2000]
- F105: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) that preserve and expose some neutralizing epitopes while occluding some non-neutralizing epitopes – CD4BS MAbs (F105 and F91) and CD4i (17b and 48d) recognized gp140-GNC4 as well as gp120 or gp140 – non-neutralizing MAbs C11, A32, 522-149, M90, and #45 bound to the gp140-GNC4 glycoprotein at reduced levels compared to gp120 – MAbs directed at the extreme termini of gp120 C1 (135/9 and 133/290) and C5 (CRA-1 and M91) bound efficiently to gp140-GNC4 [Yang2000]
- F105: SHIV-HXBc2 is a neutralization sensitive non-pathogenic virus, and several *in vivo* passages through monkies yielded highly pathogenic SHIV KU-1—HXBc2 and the KU-1 clone HXBc2P3.2 differ in 12 amino acids in gp160—substitutions in both gp120 and gp41 reduced the ability of sCD4, IgG1b12, F105 and AG1121 to Env achieve saturation and full occupancy, and neutralize KU-1—17b and 2F5 also bound less efficiently to HXBc2P3.2, although 2G12 was able to bind both comparably [Si2001].
- F105: Mutations in two glcosylation sites in the V2 region of HIV-1 ADA at positions 190 and 197 (187 DNTSYRLINCNTS 199) cause the virus to become CD4-independent and able to enter cells through CCR5 alone – these same mutations tended to increase the neutralization sensitivity of the virus, including to F105 [Kolchinsky2001]
- F105: Abs against the V3 loop (50.1, 58.2, 59.1, 257-D, 268-D, 447-52D), CD4BS (IgG1b12, 559-64D, F105), CD4i (17b), and to gp41 (2F5, F240) each showed similar binding efficiency to Env derived from related pairs of primary and TCLA lines (primary: 168P and 320SI, and TCLA: 168C and 320SI-C3.3), but the TCLA lines were much more susceptible to neutralization suggesting that the change in TCLA lines that make them more susceptible to NAbs alters some step after binding [York2001]
- F105: Uncleaved soluble gp140 (YU2 strain, R5 primary isolate) can be stabilized in an oligomer by fusion with a C-term trimeric GCN4 motif or using a T4 trimeric motif derived from T4 bacteriophage fibritin—stabilized oligomer gp140δ683(-FT) showed strong preferential recognition by NAbs IgG1b12 and 2G12 relative to the gp120 monomer, in contrast to poorly neutralizing MAbs F105, F91, 17b, 48d, and 39F which showed reduced levels of binding, and C11, A32, and 30D which did not bind the stabilized oligomer [Yang2002].
- F105: Passive immunization of neonate macaques with a combination of F105+2G12+2F5 conferred complete protection against oral challenge with SHIV-vpu+ or – the combination b12+2G12+2F5 conferred partial protection against SHIV89.6 – such combinations may be useful for prophylaxis at birth and against milk born transmission – the synergistic combination of IgG1b12, 2G12, 2F5, and 4E10 neutralized a collection of HIV clade C primary isolates [Xu2002]
- F105: A modified gp140 (gp140deltaCFI), with C-term mutations intended to mimic a fusion intermediate and stabilize trimer formation, retained antigenic conformational determinants as defined by binding to CD4 and to MAbs 2F5, 2G12, F105, and b12, and enhanced humoral immunity without diminishing the CTL response in mice injected with a DNA vaccine [Chakrabarti2002]
- F105: A series of mutational changes were introduced into the YU2 gp120 that favored different conformations – 375 S/W seems to favor a conformation of gp120 closer to the CD4-bound state, and is readily bound by sCD4 and CD4i MAbs (17b, 48d, 49e, 21c and 23e) but binding of anti-CD4BS MAbs (F105, 15e, IgG1b12, 21h and F91 was markedly reduced – IgG1b12 failed to neutralize this mutant, while neutralization by 2G12 was enhanced – 2F5 did not neutralize either WT or mutant, probably due to polymorphism in the YU2 epitope – another mutant, 423 I/P, disrupted the gp120 bridging sheet, favored a different conformation and did not bind CD4, CCR5, or CD4i antibodies, but did bind to CD4BS MAbs [Xiang2002b]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- F105: Truncation of the gp41 cytoplasmic domain of X4, R5, and X4R5 viruses forces a conformation that more closely resembles the CD4 bound state of the external Envelope, enhancing binding of CD4i MAbs 17b and 48d and of CD4BS MAbs F105, b12, and in most cases of glycosylation site dependent MAb 2G12 and the anti-gp41 MAb 246D – in contrast, binding of the anti-V2 MAb 697D and the anti-V3 MAb 694/98D were not affected – viruses bearing the truncation were more sensitive to neutralization by MAbs 48d, b12, and 2G12 – the anti-C5 MAb 1331A was used to track levels of cell surface expression of the mutated proteins [Edwards2002]
- F105: HIV-1 gp160δCT (cytoplasmic tail-deleted) proteoliposomes (PLs) containing native, trimeric envelope glycoproteins from R5 strains YU2 and JRFL, and X4 strain HXBc2, were made in a physiologic membrane setting as candidate immunogens for HIV vaccines—2F5 bound to gp160δCT with a reconstituted membrane ten-fold better than the same protein on beads, while such an affinity difference was not seen with F105 and 2G12—anti-CD4BS MAbs IgG1b12 and F105, A32 (C1-C4), C11 (C1-C5), and 39F (V3) MAbs bound gp160δCT PLs indistinguishably from gp160δCT expressed on the cell surface [Grundner2002].
- F105: gp120 mutants were used to define the CXCR4 binding site using CXCR4 displayed on paramagnetic proteoliposomes (PMPLs) to reduce non-specific gp120 binding—basic residues in the V3 loop and the β19 strand (RIKQ, positions 419-422) were involved, and deletion of the V1-V2 loops allowed CD4-independent CXCR4 binding—MAbs 17b (CD4i) and F105 (CD4BS) were used to study conformational changes in the mutants—the affinity of ΔV1 and ΔV1-V2 mutants for F105 was comparable to the wildtype—V3 mutants did not affect F105 binding—the K421A mutation in the β19 strand dramatically reduced F105 affinity, consistent with what is known about the F105 epitope [Basmaciogullari2002].
- F105: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain [Zhang2002]
- F105: Review of NAbs that notes that F105 binds the CD4BS, in combination with other MAbs it can protect some macaques against SHIV infection, and that it has strong ADCC activity [Ferrantelli2002]
- F105: Review of NAbs that discusses mechanisms of neutralization, passive transfer of NAbs and protection in animal studies, and vaccine strategies [Liu2002]
- F105: Virion capture assays are not a good preditor of neutralization, and the presentation of epitopes using this assay seems to be different from that of functional Envelope spikes on primary isolates – F105 and b6 could efficiently block the b12-mediated capture of infectious virions in a virus capture, but did not inhibit b12 neutralization – while b12 was potent at neutralizing the three primary virions JR-CSF, ADA, and 89.6, the Abs F105, 19b, and Fab b6 were overall very poor neutralizers [Poignard2003]
- F105: Alanine scanning mutagenesis was used to compare substitutions that affected anti-CD4BS NAb b12 – rec gp120s were engineered to contain combinations of Alanine substitutions that enhanced b12 binding, and while binding of b12 to these gp120 monomers was generally maintained or increased, binding by five non-neutralizing anti-CD4bs MAbs (b3, b6, F105, 15e, and F91) was reduced or completely abolished [Pantophlet2003]
- F105: NIH AIDS Research and Reference Reagent Program: 857

924	F91 (F-91)	Env	gp120		No		

Ab type CD4BS **Donor** James Robinson, University of Connecticut, Storrs

References Moore1993a, Moore1994b, Moore1996, Fouts1997, Mondor1998, Parren1998a, Binley1998, Fouts1998, Yang2000, Yang2002, Xiang2002b, Pantophlet2003

- F91: Called F-91 – neutralizes IIIB – reactive with SF-2 gp120 – strong inhibition of HIV+ human sera binding to IIIB gp120 [Moore1993a]
- F91: Has strong cross-reactivity with gp120 monomers from most subtypes, A-F [Moore1994b]
- F91: Unusual pattern of reciprocal enhancement with several anti-V2 and V3 directed MAbs – reciprocal inhibition of other CD4BS MAbs [Moore1996]
- F91: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric Env binding – F91 bound monomer, did not bind oligomer or neutralize JRFL [Fouts1997]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- F91: Weak inhibition of binding of Hx10 to CD4 positive or negative cells, weakly neutralizing [Mondor1998]
- F91: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren1998a]
- F91: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer – CD4BS MAbs 15e, F91 and IgG1b12 bound better to the deleted protein than to wild type [Binley1998]
- F91: CD4BS MAbs 15e, 21h, and F91 bind with even lower affinity than 205-43-1 and 205-42-15 to JRFL oligomer – conclusions of this paper contrast with [Parren1998a] [Fouts1998]
- F91: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) that preserve and expose some neutralizing epitopes while occluding some non-neutralizing epitopes – CD4BS MAbs (F105 and F91) and CD4i (17b and 48d) recognized gp140-GNC4 as well as gp120 or gp140 – non-neutralizing MAbs C11, A32, 522-149, M90, and #45 bound to the gp140-GNC4 glycoprotein at reduced levels compared to gp120 – MAbs directed at the extreme termini of gp120 C1 (135/9 and 133/290) and C5 (CRA-1 and M91) bound efficiently to gp140-GNC4 [Yang2000]
- F91: Uncleaved soluble gp140 (YU2 strain, R5 primary isolate) can be stabilized in an oligomer by fusion with a C-term trimeric GCN4 motif or using a T4 trimeric motif derived from T4 bacteriophage fibritin – stabilized oligomer gp140 delta683(-FT) showed strong preferential recognition by NAbs IgG1b12 and 2G12 relative to the gp120 monomer, in contrast to poorly neutralizing MAbs F105, F91, 17b, 48d, and 39F which showed reduced levels of binding, and C11, A32, and 30D which did not bind the stabilized oligomer [Yang2002]
- F91: A series of mutational changes were introduced into the YU2 gp120 that favored different conformations – 375 S/W seems to favor a conformation of gp120 closer to the CD4-bound state, and is readily bound by sCD4 and CD4i MAbs (17b, 48d, 49e, 21c and 23e) but binding of anti-CD4BS MAbs (F105, 15e, IgG1b12, 21h and F91 was markedly reduced – IgG1b12 failed to neutralize this mutant, while neutralization by 2G12 was enhanced – 2F5 did not neutralize either WT or mutant, probably due to polymorphism in the YU2 epitope – another mutant, 423 I/P, disrupted the gp120 bridging sheet, favored a different conformation and did not bind CD4, CCR5, or CD4i antibodies, but did bind to CD4BS MAbs [Xiang2002b]
- F91: Alanine scanning mutagenesis was used to compare substitutions that affected anti-CD4BS NAb b12 – rec gp120s were engineered to contain combinations of Alanine substitutions that enhanced b12 binding, and while binding of b12 to these gp120 monomers was generally maintained or increased, binding by five non-neutralizing anti-CD4bs MAbs (b3, b6, F105, 15e, and F91) was reduced or completely abolished [Pantophlet2003]

925	GP13 (ARP3054)	Env	gp120		L	HIV-1 infection	human (IgG1)

Ab type CD4BS

References

Schutten1993, Back1993, Bagley1994, Schutten1995a, Schutten1995b, Bolmstedt1996, Wisnewski1996, Schutten1996, Schutten1997, Vella2002

- GP13: Neutralized a broad range of HIV-1 strains from phylogenetically different subfamilies – the following gp120 amino acid substitutions strongly inhibit binding: 256(S/Y), 257(T/G), 262(N/T), 368(D/R or K), 370(E/R or Q or D), 384(Y/E) [Schutten1993]
- GP13: Mutations in a neutralization resistant isolate obtained by passage of the IIIB isolate in chimpanzees reduced neutralization, but the escape was not as clear as seen with anti-V3 MAbs [Back1993]
- GP13: Neutralizes IIIB – only slight inhibition of SI phenotype, and strong enhancement of NSI phenotype chimeric viruses, that incorporated different envs from the same donor [Schutten1995a]
- GP13: Neutralizes T-cell adapted viruses but not the SI strain 16.2, despite high binding affinity [Schutten1995b]
- GP13: Sera were obtained from guinea pigs vaccinated either with gp160, or with gp160 lacking N-linked glycans at N406, N448, and N463 – these sera could block equally well both the CD4 BS MAb GP13 and the V3 MAb F58/H3 [Bolmstedt1996]
- GP13: GP13 is V H5 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals [Wisnewski1996]
- GP13: IIIB neutralizing MAbs in vitro fail to neutralize in a mouse model it in vivo [Schutten1996]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• GP13: Neutralized (50%) an SI-env chimeric virus and enhanced (>5 fold) an NSI-env chimeric virus [Schutten1997] • GP13: Called ARP3054: Herpesvirus saimiri-immortalized CD4+ T lymphocytes (HVS T cells) were used to isolate virus and perform HIV-1 neutralization assays, and compared with a standard PBMC protocol – neutralization sensitivities to a panel of MAbs and to homologous or heterologous plasma/sera were similar for HVS T cells (CN-2 cells) and PBMCs [Vella2002] • GP13: UK Medical Research council AIDS reagent: ARP3054					
926	GP44	Env	gp120		L	HIV-1 infection	human (IgG1)
		Ab type CD4BS **References** Schutten1993, Bagley1994, Wisnewski1996 • GP44: Exhibited a more restricted pattern of neutralizing activity than GP13 and GP68 – the following gp120 amino acid substitutions strongly inhibit binding: 256(S/Y), 257(T/G), 262(N/T), 368(D/R or K), 370(E/R or Q or D) [Schutten1993] • GP44: GP44 is V H1 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals [Wisnewski1996]					
927	GP68	Env	gp120		L	HIV-1 infection	human (IgG1)
		Ab type CD4BS **References** Schutten1993, Klasse1993a, Bagley1994, Schutten1995a, Guillon2002 • GP68: Neutralized a broad range of HIV-1 lab strains from phylogenetically different subfamilies – the following gp120 amino acid substitutions strongly inhibit binding: 117(K/W), 256(S/Y), 257(T/G), 262(N/T), 368(D/R or K), 370(E/R or Q), 384(Y/E), 435(Y/H) [Schutten1993] • GP68: The gp41 mutation 582(Ala to Thr) results in conformational changes in gp120 that confer neutralization resistance to a class of conformation sensitive neutralizing MAbs – GP68 required markedly higher concentrations to neutralize the mutant than wild type [Klasse1993a] • GP68: Neutralizes IIIB – only slight inhibition of SI phenotype, and strong enhancement of NSI phenotype chimeric viruses, that incorporated different envs from the same donor [Schutten1995a] • GP68: GP68 is V H1 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals [Wisnewski1996] • GP68: The affect of Ab binding on infectivity was studied by pseudotyping three related envs with different phenotypes – R5 viruses were preferentially enhanced, not X4 – the V3 region was the main determinant of Ab-mediated enhancement and modulation of the interaction between CCR5 and gp120 is critical – tests with MAbs anti-V3 391/95-D and CD4BS-specific GP68 indicate that Ab specificity did not determine whether or not infectivity was enhanced or neutralized, rather the phenotype was determined by Envelope conformation [Guillon2002] • GP68: UK Medical Research Council AIDS reagent: ARP3055					
928	HF1.7	Env	gp120		L	anti-idiotype	murine (IgM)
		Ab type CD4BS **References** Chanh1987 • HF1.7: An anti-Id antibody stimulated by anti-CD4 MAb Leu-3a binds to recombinant gp160, suggesting HF1.7 mimics CD4 [Chanh1987]					
929	HT5	Env	gp120		L (weak)	HIV-1 infection	human
		Ab type CD4BS **Donor** Ciba-Geigy AG (Basel, Switzerland), and Tanox Biosystems, Houston, Texas **References** Moore1994b, Moore1995a, Fouts1997, Fouts1998, Herrera2003 • HT5: HT5, HT6, and HT7 are also known as 205-43-1, 205-42-15, and 205-46-9, respectively [Fouts1998] • HT5: Despite highly cross-reactive binding to many primary and T-cell adapted viral strains, only weakly neutralizes IIIB and MN [Moore1995a] • HT5: 205-46-9 was cross-reactive across clades A-F, 205-43-1 very cross-reactive but not quite as extensive 205-46-9 [Moore1994b] • HT5: MAbs IgG1b12, HT5, HT6, and HT7 cross-compete for binding to monomeric gp120, bind equally well, inhibit gp120-sCD4 interactions, but only IgG1b12 neutralizes JRFL [Fouts1997]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- HT5: HT5 and HT6 bind JRSF oligomer but with low affinity, and are not neutralizing – conclusions of this paper contrast with [Parren1998a] [Fouts1998]
- HT5: Called 205-43-1 – CD4BS MAbs b12 (neutralizing) and 205-42-15, 204-43-1, 205-46-9 (nonneutralizing) all cross-competed for binding to monomeric gp120, indicating the topological proximity of their epitopes, however, the nonneutralizing CD4BS MAbs did not interfere with the neutralization activity of MAb b12 – the nonneutralizing MAbs partially competed with b12 for Env binding of the surface of Env-transfected cells – this suggests Env has two categories of binding site for CD4BS MAbs, one recognized by both b12 and nonneutralizing CD4BS MAbs, the other is recognized by only b12 – Ab-gp120 interactions based on the use of monomeric gp120 or Env-transfected cells do not predict the outcome of HIV-1 neutralization assays, and they should be interpreted with caution [Herrera2003]

930	HT6	Env	gp120		L (weak)	HIV-1 infection	human

Ab type CD4BS **Donor** Ciba-Geigy AG Basel, Switzerland, and Tanox Biosystems, Houston, Texas
References Moore1994b, Moore1995a, Fouts1997, Fouts1998, Herrera2003

- HT6: HT5, HT6, and HT7 are also known as 205-43-1 , 205-42-15, and 205-46-9, respectively [Fouts1998]
- HT6: Despite highly cross-reactive binding to many primary and T-cell adapted viral strains, only weakly neutralizes IIIB and MN [Moore1995a]
- HT6: 205-46-9 was cross-reactive across clades A-F, 205-43-1 was not quite as extensively cross-reactive [Moore1994b]
- HT6: MAbs IgG1b12, HT5, HT6, and HT7 cross-compete for binding to monomeric gp120, bind equally well, inhibit gp120-sCD4 interactions, but only IgG1b12 neutralizes JRFL [Fouts1997]
- HT6: HT5 and HT6 bind JRSF oligomer but with low affinity, and are not neutralizing – conclusions of this paper contrast with [Parren1998a] [Fouts1998]
- HT6: Called 205-42-15 – CD4BS MAbs b12 (neutralizing) and 205-42-15, 204-43-1, 205-46-9 (nonneutralizing) all cross-competed for binding to monomeric gp120, indicating the topological proximity of their epitopes, however, the nonneutralizing CD4BS MAbs did not interfere with the neutralization activity of MAb b12 – the nonneutralizing MAbs partially competed with b12 for Env binding of the surface of Env-transfected cells – this suggests Env has two categories of binding site for CD4BS MAbs, one recognized by both b12 and nonneutralizing CD4BS MAbs, the other is recognized by only b12 – Ab-gp120 interactions based on the use of monomeric gp120 or Env-transfected cells do not predict the outcome of HIV-1 neutralization assays, and they should be interpreted with caution [Herrera2003]

931	HT7	Env	gp120		L (IIIB)	HIV-1 infection	human

Ab type CD4BS **Donor** Ciba-Geigy AG (Basel, Switzerland), and Tanox Biosystems, Houston, Texas
References Moore1994b, Moore1995a, Fouts1997, Fouts1998, Herrera2003

- HT7: HT5, HT6, and HT7 are also known as 205-43-1 , 205-42-15, and 205-46-9, respectively [Fouts1998]
- HT7: Despite highly cross-reactive binding to many primary and T-cell adapted viral strains, only neutralizes IIIB well, with sporadic weak neutralization of other isolates [Moore1995a]
- HT7: 205-46-9 was cross-reactive across clades A-F, 205-43-1 was cross-reactive, but not quite as extensive [Moore1994b]
- HT7: MAbs IgG1b12, HT5, HT6, and HT7 cross-compete for binding to monomeric gp120, bind equally well, inhibit gp120-sCD4 interactions, but only IgG1b12 neutralizes JRFL [Fouts1997]
- HT7: Binds JRSF oligomer with high affinity, at least as high as IgG1b12, but IgG1b12 is neutralizing, H7 is not – conclusions of this paper contrast with [Parren1998a] – authors propose a model where H7 may inhibit CD4 binding, but cause a conformational shift which enhances CCR5 binding and thus counteracts the neutralizing effect [Fouts1998]
- HT7: Called 205-46-9 – CD4BS MAbs b12 (neutralizing) and 205-42-15, 204-43-1, 205-46-9 (nonneutralizing) all cross-competed for binding to monomeric gp120, indicating the topological proximity of their epitopes, however, the nonneutralizing CD4BS MAbs did not interfere with the neutralization activity of MAb b12 – the nonneutralizing MAbs partially competed with b12 for Env binding of the surface of Env-transfected cells – this suggests Env has two categories of binding site for CD4BS MAbs, one recognized by both b12 and nonneutralizing CD4BS MAbs, the other is recognized by only b12 – Ab-gp120 interactions based on the use of monomeric gp120 or Env-transfected cells do not predict the outcome of HIV-1 neutralization assays, and they should be interpreted with caution [Herrera2003]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
932	ICR 39.13g (ICR39.13g, 39.13g)	Env	gp120		L	Vaccine	rat (IgG2b)

Vaccine *Vector/Type:* recombinant protein *Strain:* BH10 *HIV component:* gp120
Ab type CD4BS **Donor** Jackie Cordell and C. Dean
References Cordell1991, McKeating1992a, McKeating1992c, McKeating1993b, Moore1993a, Thali1993, Klasse1993a, McLain1994, Beretta1994, McKeating1996b, Armstrong1996a, Klasse1996, Peet1998, Vella2002

- ICR 39.13g: Cross-competes with MAbs ICR 39.3b and 15e [Cordell1991]
- ICR 39.13g: Binds to a conformational epitope involved in CD4 binding – exerts a synergistic effect in combination with V3 directed MAbs [McKeating1992a]
- ICR 39.13g: Neutralization activity against HXB10, RF, SF-2 and MN strains of HIV-1 [McKeating1993b]
- ICR 39.13g: Conformational, does not bind denatured gp120 – weak neutralization of IIIB – strong inhibition of HIV+ human sera binding to IIIB gp120 [Moore1993a]
- ICR 39.13g: Strongly inhibits CD4 inducible MAb 48d [Thali1993]
- ICR 39.13g: Kinetics of neutralization studied – no lag for 39.3b, while ICR 39.13g and ICR 41.1i have lags of 5 and 15 min respectively – mediates neutralization with 2.3 molecules of IgG [McLain1994]
- ICR 39.13g: The gp41 mutation 582(Ala to Thr) results in conformational changes in gp120 that confer neutralization resistance to a class of conformation sensitive neutralizing MAbs – ICR 39.13g required moderately higher concentrations to neutralize the mutant than wild type [Klasse1993a]
- ICR 39.13g: Called 39.13g Neutralizes HXB2, but fails to neutralize chimeric virus with gp120 from primary isolates in an HXB2 background [McKeating1996b]
- ICR 39.13g: Post-attachment neutralization mechanism, in contrast to MAb 39.3b [Armstrong1996a]
- ICR 39.13g: Variants of LAI have differing neutralization susceptibility to 39.13g [Klasse1996]
- ICR 39.13g: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind – ICR 39.13g was not affected by V3 serine substitutions – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions [Peet1998]
- ICR 39.13g: Called ARP390/391, but no such entry was found at the UK Medical Research Council AIDS reagent web site: Herpesvirus saimiri-immortalized CD4+ T lymphocytes (HVS T cells) were used to isolate virus and perform HIV-1 neutralization assays, and compared with a standard PBMC protocol – neutralization sensitivities to a panel of MAbs and to homologous or heterologous plasma/sera were similar for HVS T cells (CN-2 cells) and PBMCs [Vella2002]
- ICR 39.13g: UK Medical Research Council AIDS reagent: ARP390

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
933	ICR 39.3b (39.3, 39.3b, ICR39.3b)	Env	gp120		L	Vaccine	rat (IgG2b)

Vaccine *Vector/Type:* recombinant protein *Strain:* BH10 *HIV component:* gp120
Ab type CD4BS **Donor** J. Cordell and C. Dean
References Cordell1991, McKeating1992c, Moore1993c, McLain1994, Armstrong1996a, Jeffs1996, Wyatt1998a

- ICR 39.3b: also known as 39.3, 39.3b and ICR39.3b
- ICR 39.3b: Cross-competes with MAbs ICR 39.13g and 15e [Cordell1991]
- ICR 39.3b: Conformational, does not bind to denatured IIIB [Moore1993a]
- ICR 39.3b: Kinetics of neutralization studied – no lag for 39.3b, while ICR 39.13g and ICR 41.1i have lags of 5 and 15 min respectively [McLain1994]
- ICR 39.3b: Neutralizes only if the antibody is added prior to the attachment of the virus to the cell, in contrast to 39.13g [Armstrong1996a]
- ICR 39.3b: Called 39.3b – increased binding when V1/V2 or V1/V2 and V3 were deleted from gp120 [Jeffs1996]
- ICR 39.3b: Called 39.3 – summary of the implications of the crystal structure of the core of gp120 bound to CD4 and 17b with what is known about mutations that reduce NAb binding – probable mechanism of neutralization by CD4BS Ab is direct interference with CD4 binding [Wyatt1998a]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• ICR 39.3b: UK Medical Research Council AIDS reagent: ARP391					
934	IgG1b12 (Fab b12, Fab 3B3, MAb IgG1b12, IgG1-b12, IgG1 b12, IgGB12, b4/12, b12, 1b12, immunoglobulin G1b12, ARP3065, IgG1 b12)	Env	gp120		L P	HIV-1 infection	human (IgG1κ)

Ab type CD4BS **Donor** D. Burton, Scripps Research Institute, La Jolla, CA, also J. Geltowsky and J. Pyati, R. W. Johnson Pharmaceutical Research Inst. La Jolla, CA

References Burton1991, Barbas III1992, Roben1994, Burton1994, Moore1994b, Sattentau1995a, Moore1995a, Moore1995b, Parren1995, Trkola1995, Ditzel1995, Sullivan1995, Yang1997c, Moore1996, Gauduin1996, Poignard1996b, Poignard1996a, Trkola1996a, Sattentau1996, McKeating1996a, D'Souza1997, Schutten1997, Mo1997, Fouts1997, Li1997, Kessler II1997, Moore1997, Stamatatos1997, Ditzel1997, Ugolini1997, Wyatt1997, Burton1997, Boots1997, Parren1997c, Parren1997b, Parren1997a, Valenzuela1998, Wyatt1998a, Mondor1998, Parren1998a, Connor1998, Binley1998, Fouts1998, Takefman1998, Parren1998b, Brand1998, Schonning1998, Sullivan1998a, Frankel1998, Kropelin1998, Stamatatos1998, Poignard1999, Jackson1999, Hioe1999, Montefiori1999, Giraud1999, Beddows1999, Binley1999, Grovit-Ferbas2000, Ly2000, Nyambi2000, Park2000, Si2001, Kolchinsky2001, Saphire2001a, Saphire2001b, Yang2001, York2001, Zwick2001a, Zwick2001b, Zwick2001c, Parren2001, Poignard2001, Zeder-Lutz2001, Spenlehauer2001, Verrier2001, Hofmann-Lehmann2001, Xu2001, Srivastava2002, Golding2002b, Sanders2002, Schulke2002, Yang2002, Saphire2002, Scanlan2002, Xu2002, Chakrabarti2002, Vella2002, Xiang2002b, Edwards2002, Grundner2002, Zhang2002, Klasse2002, Ferrantelli2002, Liu2002, Poignard2003, Pantophlet2003, Herrera2003

- IgG1b12: Fab b12 was derived from IgG1b12, Fab 3B3 was derived from Fab b12 by random mutagenesis and selected for increased affinity to sgp120 – database note
- IgG1b12: The original Fab fragment was derived from a combinatorial phage library from bone marrow of an HIV-1 positive individual who had been asymptomatic for six years [Burton1991]
- IgG1b12: Anti-CD4 binding site Fab, potent neutralizing activity, greater affinity for a subpopulation of gp120 molecules suggested to be in a mature confirmation – mutations in gp120 that abrogate binding: 368 D/R or D/T, 370 E/R, and 477 D/V, of clone HXBc2 of LAI – sensitive to V1 and V2 substitutions [Roben1994]
- IgG1b12: Very potent neutralization, of primary and lab strains, at concentrations that could be achieved by passive immunization – reduced binding with A,C, and D clade viruses relative to B clade, poor reactivity with E clade – isolates that were refractive to neutralization by sera from HIV-1+ donors could be neutralized by IgG1 b12 [Burton1994]
- IgG1b12: Cross-reactive with some gp120s, (but not all), from clades A-D – not reactive with gp120 from clades E or F [Moore1994b]
- IgG1b12: Formalin inactivation of virus at 0.1% formalin for 10 hours at 4 degrees was optimal for inactivation of virus while maintaining epitope integrity [Sattentau1995c]
- IgG1b12: Anti-CD4 binding site MAb – very potent neutralization of a number of primary isolates [Moore1995a]
- IgG1b12: Complete protection against HIV-1 infection was achieved in hu-PBL-SCID mice by passive immunization with physiologically relevant doses – pharmacokinetics showed serum half-life of 30.2 +/- 1.3 hours for Fab b12 and 7.4 +/- 0.7 days for IgG1 b12 in mice, but IgG1 half-lives in human are generally between 21-23 days [Parren1995, Parren1997a]
- IgG1b12: Called BM12 – broad cross-clade neutralization of primary isolates – additive neutralization in combination with MAb 2F5 [Kessler1995]
- IgG1b12: Review: unusual properties for anti-CD4 BS MAb: sensitive to V2 substitutions, preferential recognition of the oligomer on the cell surface [Moore1995b]
- IgG1b12: Could potently neutralize primary isolates from within clade B, but showed a slight reduction in efficacy outside of clade B [Trkola1995]
- IgG1b12: Because Fab b12 shows reduction in binding when the V2 loop is deleted and when aa 183/184 PI/SG substitutions are made competition studies were done with Fab L78 and anti-V2 MAbs SC258 and 684-238 and they do not compete with IgG1b12 [Ditzel1995]
- IgG1b12: Fab b12 showed potent neutralization of T-cell-line-adapted strains, but much reduced neutralization of 3 primary isolates – 2 of the 3 primary isolates also had reduced binding affinity, but the third was as efficiently immunoprecipitated as HXBc2 [Sullivan1995]
- IgG1b12: Saturation mutagenesis of the complementarity-determining region and optimization strategies were used to create very high affinity versions of this Fab – increased affinity was dominated by a slowing of the off rate [Yang1997c]

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- IgG1b12: Potent neutralizing ex vivo of virus taken directly from plasma of HIV-1 infected individuals – little correlation between neutralization sensitivity of passaged virus and plasma derived virus – more effective than MAb 19b [Gauduin1996]
- IgG1b12: Review: Unique among anti-CD4BS MAbs in terms of being potent against both lab adapted virus and primary isolates – one of three MAbs (IgG1b12, 2G12, and 2F5) generally accepted as having significant potency against primary isolates [Poignard1996b]
- IgG1b12: Anti-CD4BS MAbs 15e, 21h, and IgG1b12 did not cause gp120 dissociation from virus, or exposure of the gp41 epitope of MAb 50-69, in contrast to CD4i MAb 48d and anti-V3 neutralizing MAbs [Poignard1996a]
- IgG1b12: Neutralizes JR-FL – inhibits gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study [Trkola1996a]
- IgG1b12: Review: Only four epitopes have been described which can stimulate a useful neutralizing response to a broad spectrum of primary isolates, represented by the binding sites of MAbs: 447-52-D, 2G12, Fab b12, and 2F5 [Sattentau1996]
- IgG1b12: In a multilab evaluation of monoclonal antibodies, only IgG1b12, 2G12, and 2F5 could neutralize at least half of the 9 primary test isolates at a concentration of < 25 mug per ml for 90% viral inhibition – IgG1b12 failed to neutralize only 1/9 primary isolates, although there was some variation between test sites [D'Souza1997]
- IgG1b12: Inhibited some SI- and NSI-env chimeric viruses but enhanced one NSI-env chimeric virus 3 fold [Schutten1997]
- IgG1b12: JRCSF was cultured in the presence of IgG1b12 until a 100-fold resistance to neutralization was selected – resistance was due to three changes: V2 substitution D182N and C3 substitution P365L conferred resistance, and V2 D164N was also required for a viable virus – IgG1b12 resistant virus remained sensitive to MAbs 2G12 and 2F5 [Mo1997]
- IgG1b12: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric Env binding – IgG1b12 bound monomer, oligomer, and neutralized JRFL [Fouts1997]
- IgG1b12: b12 was used in its IgG1 form – of 14 human MAbs, the most potent neutralizer of SHIV-vpu+, which expressed HIV-1 IIIB env – all Ab combinations tested showed synergistic neutralization – b12 has a synergistic response with MAbs 694/98-D (anti-V3), 2F5, and 2G12 [Li1997]
- IgG1b12: 35 primary isolates were tested and all were neutralized by IgG1b12 (including 4, UG270, RW92/026, ZB20, and 301727 which been had reported as not neutralized by IgG1b12 [Trkola1995]) – IgG1b12 could neutralize even when added after the virus to the culture – selection for 400-fold increased affinity did not enhance neutralization by antibody – IgG1b12 was more potent with greater breadth than MAb 2F5 [Kessler II1997]
- IgG1b12: Review: MAbs 2F5, 2G12 and IgG1b12 have potential for use in combination with CD4-IgG2 as an immunotherapeutic or immunoprophylactic – homologous MAbs to these are rare in humans and vaccine strategies should consider including constructs that may enhance exposure of these MAbs' epitopes [Moore1997]
- IgG1b12: Viral binding inhibition by IgG1b12 strongly correlated with neutralization (all other neutralizing MAbs tested showed some correlation except 2F5) [Ugolini1997]
- IgG1b12: Major deletions in C1 and C5 and deletions of the V1V2 and V3 loops do not diminish binding [Wyatt1997]
- IgG1b12: This is a review that includes a description of IgG1b12, noting approximately equivalent affinities for sgp120 and unprocessed gp160, and somewhat enhanced affinity for the native oligomer on TCLA viruses – primary viruses have reduced affinity, but still in the useful range for neutralization – there can be complete protection in hu-PBL-SCID mice with Ab even when administered several hours after viral challenge – competes with sCD4, but unlike other CD4BS antibodies, it is sensitive to mutations in V2 [Burton1997]
- IgG1b12: In this review, the technique and potential application of Fab expression and selection in phage display libraries, and subsequent production of IgG molecules is discussed – b12 is exceptionally potent at neutralization and can successfully neutralize most B clade primary isolates, and many isolates from other subtypes as well – 3B3 was derived from b12 by selection for higher affinity using the CDR walking strategy – 3B3 has 8-fold enhancement of binding, a linear correlation was found between neutralization and affinity, and 3B3 can neutralize strains b12 cannot [Parren1997a]
- IgG1b12: Abs that recognize discontinuous epitopes can identify mimotopes from a phage peptide display library – IgG1b12 blocks CD4 binding and is the most potent neutralizing Ab – many 15 and 21-mer phage inserts were recognized, but it was not possible to derive a consensus – common features were a W and at least one acidic residue, and one sequence was found multiple times: NWPRWWEEFVDKHSS, and this peptide could compete with gp120 – two short stretches found in the phage peptides might mimic gp120 components of the epitope: positions 382-384, FFY(I), and 423-426 I(FV)I(V)NM [Boots1997]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- IgG1b12: Fab b12 is unusual in that it binds to gp140 and monomeric gp120 with similar affinities, and with a higher affinity to the native oligomer—authors propose this antibody may be exceptional because it binds the virus rather than viral debris—IgG1b12 can protect against infection prior to or shortly after challenge of hu-PBL-SCID mice with TCLA strains and primary strains, but the serum concentrations required *in vivo* were higher than for *in vitro* neutralization [Parren1997c, Parren1997b].
- IgG1b12: MAb was slightly more efficient at neutralization than Fab – inhibits viral binding to cells and viral entry – doesn't affect CD4-independent binding to T-cells [Valenzuela1998]
- IgG1b12: Summary of the implications of the crystal structure of the core of gp120 bound to CD4 and 17b with what is known about mutations that reduce NAb binding – probable mechanism of neutralization by CD4BS Ab is direct interference with CD4 binding – IgG1b12 is an unusual CD4BS antibody because it is particularly potent as a neutralizing antibody and it is susceptible to changes in the V1-V2 stem loop structure, and so it may disrupt an interaction between CD4 and conserved amino acids on the V1-V2 stem [Wyatt1998a]
- IgG1b12: Enhances binding of Hx10 to CD4 positive or negative HeLa cells, inhibits binding to CD4+ T-cell line A3.01 – neutralizes HeLa and A3.01 cell Hx10 infection [Mondor1998]
- IgG1b12: IgG1b12, Fab b12 and 3B3 derived from b12 were all included in this study – the rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142-10 > DA48 > L17) was markedly different than Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142-10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope – binding affinity of divalent IgG1b12 is 17-fold greater than monovalent Fab b12 [Parren1998a]
- IgG1b12: Ab from gp120 vaccinated individuals prior to infection, who subsequently became HIV infected, could not achieve 90% neutralization of the primary virus by which the individuals were ultimately infected – these viruses were not particularly refractive to neutralization, as determined by their susceptibility to neutralization by MAbs 2G12, IgG1b12, 2F5 and 447-52D [Connor1998]
- IgG1b12: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer – CD4BS MAbs 15e, F91 and IgG1b12 bound better to the deleted protein than to wild type [Binley1998]
- IgG1b12: Binds JRSF oligomer with high affinity, as do 205-46-9 and 2G6, but IgG1b12 is neutralizing, the other two are not – conclusions of this paper contrast with Parren98 – authors propose a model where 205-46-9 and 2G6 may inhibit CD4 binding, but cause a conformational shift which enhances CCR5 binding and thus counteracts the neutralizing effect – rank order of CD4BS antibodies oligomer binding is IgG1b12 = 2G6 = 205-46-9 > 205-43-1 = 205-42-15 > 15e = 21h = F91, and the only thing notably distinguishing about neutralizing IgG1b12 is that it depends on residues in V2 [Fouts1998]
- IgG1b12: Induces Complement-mediated lysis in MN but not primary isolates – primary isolates are refractive to CML [Takefman1998]
- IgG1b12: MAbs 2G12, 2F5 and b12 are broadly neutralizing, as are some human polyconal sera, but this paper describes a set of primary isolates that are resistant to all three MAbs and 2 broadly neutralizing sera – results indicate that resistance levels of pediatric isolates might be higher than adult isolates – resistance in general did not seem to be conferred by a loss of binding affinity for gp120 or gp41, rather by a more global perturbation of oligomeric Envelope [Parren1998b]
- IgG1b12: Immunoprecipitation of gp120 and gp160 expressed from a rec Semliki Forest virus by F105 and IgG1b12 indicated that the SFV expressed HIV-1 Env was folded appropriately – and SVF-HIV-1 Env vaccine gave the strongest anti-HIV-1 Env response in mice, when compared to an HIV-1 Env DNA vaccine and a rgp160 protein [Brand1998]
- IgG1b12: MAbs 654-D100 and IgG1b12 neutralized viruses HIV-BRU and a mutated virus that lacks the V3 loop glycan equally effectively – in contrast, sera from guinea pigs immunized with BRU gp120 neutralize viruses more effectively that lack the V3 glycan[Schonning1998]
- IgG1b12: Fab b12 – the HIV-1 virus YU2 entry can be enhanced by MAbs binding to the CD4BS, V3 loop, and CD4i epitopes – the activation for this enhanced entry state could be conferred on HxB2 by introducing the YU2 V3 loop, or the YU2 V3 and V1/V2 loops – a similar effect is observed by sub-neutralizing concentrations of sCD4 and the effect is dependent of CCR5 – Fab fragment b12 also enhances YU2 entry, ruling out Fc interactions or Env cross-linking as a mechanism, while neutralizing HXBc2 [Sullivan1998a]

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- IgG1b12: anti-C1 region MAb 87-135/9 blocks gp120 interaction with CD4+ cells – blocking activity is additive when combined with antibodies which bind in the C4 region of gp120 (F105, 388/389, and b12) [Kropelin1998]
- IgG1b12: Deleting the V2 loop of neutralization-resistant HIV-1 isolate SF162 does not abrogate its replication in PBMC or macrophages, but it enhances its neutralization sensitivity to sera from patients with B clade infection up to 170-fold, and also enhances sensitivity to sera from clades A through F – deletion of V2, but not V1, diminished neutralization by CD4BS MAb IgG1b12, in contrast to 654.30D and IgGCD4 [Stamatatos1998]
- IgG1b12: Infection of dendritic cells cultured from CD14+ blood cells or from cadaveric human skin was blocked by neutralizing MAbs IgG1b12, or 2F5 and 2G12 delivered together, but not by control non-neutralizing anti-gp120 MAb 4.8D, indicating that NAbs could interrupt early mucosal transmission events [Frankel1998]
- IgG1b12: The presence of leukocyte function-associated molecule 1 (LFA-1) promotes virus infectivity and hinders neutralization, and anti-LFA-1 MAbs can enhance the neutralizing effect of anti-HIV V3 MAb 447-52D and anti-HIV CD4BS MAb IgG1b12 – non-neutralizing anti-HIV CD4BS MAb 654-D did not become neutralizing in the presence of anti-LFA-1 MAbs [Hioe1999]
- IgG1b12: rgp120 derived from a R5X4 subtype B virus was used to vaccinate healthy volunteers and the resulting sera were compared with sera from HIV-1 positive subjects and neutralizing MAbs – TCLA strains showed enhanced IgG1b12 neutralization sensitivity relative to PBMC-adapted lines – IgG1b12 was able to bind, with low affinity, to the rgp120 monomer HIV-1 W61D [Beddows1999]
- IgG1b12: A meeting summary presented results regarding neutralization – D. Burton and J. Mascola presented results concerning passive immunization and protection of hu-PBL-SCID mice and macaques, respectively, and both found combinations of MAbs that were able to achieve 99% neutralization in vitro corresponded to efficacy in vivo [Montefiori1999]
- IgG1b12: does not inhibit attachment of virus to cells and was used as a control of a study of neutralization by a MAb F58 based micro antibody [Jackson1999]
- IgG1b12: Hu-PBL-SCID mice were infected with HIV-1s JRCSF and SF162 to study the effect of NAbs on an established infection – at day 6 post infection, mice were given 50 mg/kg of b12, an amount that would have been protective if given up to 8 hours post-infection, and 100-fold higher than the amount required for 90% neutralization in vitro – no significant differences in the initial rate of decrease in viral load or the plateau levels of viral RNA between the b12 treated and control mice were seen – in most of the Ab treated mice escape mutants were observed with varying patterns of mutations – a combination of b12, 2G12 and 2F5 protected 1/3 mice, and an isolate from one of the other two was resistant to neutralization by all three MAbs [Poignard1999]
- IgG1b12: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes [Binley1999]
- IgG1b12: To determine the antigenicity of virus killed by thermal and chemical inactivation, retention of conformation-dependent neutralization epitopes was examined, and exposure of CD4BS epitopes was found to be enhanced (MAbs IgG1b12, 205-46-9, and 205-43-1) – binding to 2G12 and 447-52D epitopes was essentially unaltered – the 17b CD4i epitope was also exposed [Grovit-Ferbas2000]
- IgG1b12: SF162 is a neutralization-resistant HIV-1 isolate – N-linked glycosylation modifications in the V2 loop of the SF162 gp120 revealed that these sites prevent neutralization by CD4BS MAbs (IgG1b12 and IgGCD4), and protect against neutralization by V3 MAbs (447-D and 391-95D) – V2-region glycosylation site mutations did not enhance neutralization resistance to V2 MAbs (G3.4 and G3.136) or CD4i MAbs (17b and 48d) – V2 glycosylation site modification allows increased infection of macrophages, probably due to glycosylated forms requiring fewer CCR5 molecules for viral entry [Ly2000]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- IgG1b12: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 CD4BS MAbs – CD4BS MAbs bound consistently to most isolates of clade D, but poorly to isolates of other clades with the exception of broadly reactive MAb IgG1b12, binding to 22 of 26 isolates tested – 8 MAbs were tested for neutralization and MAb IgG1b12 was most potent, with 90% neutralization of 3/5 isolates tested [Nyambi2000]
- IgG1b12: Fab b12 was used – six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20-100 fold more efficient at neutralizing the sensitive form – the mutation L544P reduced binding of all MAbs against gp120 by causing conformational changes [Park2000]
- IgG1b12: SHIV-HXBc2 is a neutralization sensitive non-pathogenic virus, and several in vivo passages through monkey's yielded highly pathogenic SHIV KU-1 – HXBc2 and the KU-1 clone HXBc2P3.2 differ in 12 amino acids in gp160 – substitutions in both gp120 and gp41 reduced the ability of sCD4, IgG1b12, F105 and AG1121 to Env achieve saturation and full occupancy, and neutralize KU-1 – 17b and 2F5 also bound less efficiently to HXBc2P3.2, although 2G12 was able to bind both comparably [Si2001]
- IgG1b12: Mutations in two glcosylation sites in the V2 region of HIV-1 ADA at positions 190 and 197 (187 DNTSYRLINCNTS) cause the virus to become CD4-independent and able to enter cells through CCR5 alone – these same mutations tended to increase the neutralization sensitivity of the virus, except the mutation 197 S/R which resulted in a carbohydrate addition to 195 N that disrupts the IgG1b12 binding site [Kolchinsky2001]
- IgG1b12: This paper describes the technical aspects of the crystallization of b12 at a resolution of 2.7 angstroms with all 12 Ig domains resolved [Saphire2001a]
- IgG1b12: This paper describes the biological implications of the crystal structure of b12 – a remarkable feature of this antibody is a long protruding finger-like CDR H3 that can dock in the recessed CD4-binding site – a contact residues in gp120 are modeled, with numbering based on the variable loop-deleted crystal structure of gp120 [Saphire2001b]
- IgG1b12: Primary isolates YU2 and ADA are more resistant to IgG1b12 neutralization than HXBc2: 90% Neutralization of HXBc2 is observed with 1.25 ug of IgG1b12, while ADA and YU2 require 2.5 and 5 ug respectively to achieve 50% neutralization, and 90% neutralization could not be achieved with 10 or 20 ug of IgG1b12, respectively [Yang2001]
- IgG1b12: Abs against the V3 loop (50.1, 58.2, 59.1, 257-D, 268-D, 447-52D), CD4BS (IgG1b12, 559-64D, F105), CD4i (17b), and to gp41 (2F5, F240) each showed similar binding efficiency to Env derived from related pairs of primary and TCLA lines (primary: 168P and 320SI, and TCLA: 168C and 320SI-C3.3), but the TCLA lines were much more susceptible to neutralization suggesting that the change in TCLA lines that make them more susceptible to NAbs alters some step after binding [York2001]
- IgG1b12: b12 recognizes a conformational epitope that overlaps with the CD4 binding site – a phage displayed peptide library was used to identify a peptide which bound b12, called B2.1, which competes with b12 in competition assays – B2.1 has significant homology to the D loop of gp120: upper case letters indicate residues B2.1 shares with gp120, heRsymFSDlenrcI – one of the goals of defining peptide mimics to the b12 epitope is to develop an immunogen that can stimulate b12-like antibodies, but B2.1 cross-linked to phage and ovalbumin bound IgG1b12 did not elicit cross-reactive gp120 Abs in mice or rabbits [Zwick2001a]
- IgG1b12: This paper primarily concerns 4E10 and Z13, MAbs that both bind proximally to the 2F5 binding site to a conserved epitope, and that neutralize some primary isolates from clades B, C, and E – broadly neutralizing MAbs 2F5, IgG1b12, and 4E10 and Z13 fail to neutralize different subsets of viruses [Zwick2001b]
- IgG1b12: Neutralization synergy between anti-HIV NAbs b12, 2G12, 2F5, and 4E10 was studied – a classic fixed-ratio method was used, as well as a method where one Ab was fixed at a low neutralization titer and the other was varied – using primary isolates, a two-four fold enhancement of neutralization was observed with MAb pairs, and a ten-fold enhancement with a quadruple Ab combination – no synergy was observed with any MAb pair in the neutralization of TCLA strain HXB2 – whole IgG1b12 and b12 Fab fragments behaved similarly in the neutralization assays – there was no evidence for cooperativity of binding between b12 and 2G12 to envelope spikes expressed on the cell surface of TCLA or primary isolates [Zwick2001c]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- IgG1b12: Intravenous passive transfer of MAb b12 provides dose-dependent protection from infection to macaques vaginally challenged with the R5 virus SHIV(162P4) – the primary isolate HIV-1SF162 is neutralized 90% (IC90) by b12 at 2 μg/ml, and SHIV162P4, derived from HIV-1SF162, was neutralized by 90% at 2 μg/ml in PHA-activated PBMC from rhesus macaques – the 90% neutralization titers achieved in three groups of animals that were given 25-, 5-, and 1-mg/kg doses were approximately 1:400, 1:80, and 1:16, respectively – the half-life of IgG1 b12 in plasma was about 1 week, but while the peak b12 plasma concentration was immediately after the infusion, the peak vaginal fluid concentration was 7-14 days later [Parren2001]
- IgG1b12: Structural aspects of the interaction of neutralizing Abs with HIV-1 Env are reviewed – Env essentially has three faces, one is largely inaccessible on the native trimer, and two that exposed but have low immunogenicity on primary viruses – neutralization is suggested to occur by inhibition of the interaction between gp120 and the target cell membrane receptors as a result of steric hindrance and it is noted that the attachment of approximately 70 IgG molecules per virion is required for neutralization, which is equivalent to about one IgG molecule per spike – the 2G12, 17b and b12 epitopes are discussed in detail – the structure of CD4-bound gp120 reveals features that HIV has evolved to escape anti-CD4BS Abs like IgG1b12 despite profound functional constraints – CD4BS Abs must first access the CD4 binding site, deeply recessed within the gp120 core, and the Fab of an Ab molecule is "wider" than CD4, and in addition the binding site is flanked by variable and glycosylated regions [Poignard2001]
- IgG1b12: Neutralizing synergy between MAbs 1b12, 2G12 and 2F5 was studied using surface plasmon resonance to determine the binding kinetics for these three MAbs with respect to monomeric and oligomeric env protein gp160 IIIB – the 2G12 epitope is highly accessible on both monomeric and oligomeric Envs, 1b12 is highly accessible on monomers but not oligomers, and 2F5 on neither form – binding of 2G12 exposes the 2F5 epitope on gp160 oligomers [Zeder-Lutz2001]
- IgG1b12: A luciferase-reporter gene-expressing T-cell line was developed to facilitate neutralization and drug-sensitivity assays – luciferase and p24 antigen neutralization titer end points were found comparable using NAb from sera from HIV+ donors, and MAbs 2F5, 2G12 and IgG1b12 [Spenlehauer2001]
- IgG1b12: A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6 – six gave significant neutralization at 2 to 10 ug/ml: 2F5, 50-69, IgG1b12, 447-52D, 2G12, and 670-D six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98-6, and 1281 – no synergy, only additive effects were seen for pairwise combinations of MAbs, and antagonism was noted between gp41 M Abs 50-69 and 98-6, as well as 98-6 and 2F5 [Verrier2001]
- IgG1b12: A combination of MAbs IgG1b12, 2F5, and 2G12 was given postnatally to four neonates macaques that were then challenged with highly pathogenic SHIV89.6P – one of the four infants remained uninfected after oral challenge, two infants had no or a delayed CD4(+) T-cell decline – the most potent combination included IgG1b12, which alone does not alone neutralize SHIV89.6P [Hofmann-Lehmann2001]
- IgG1b12: Twenty HIV clade C isolates from five different countries were susceptible to neutralization by anti-clade B MAbs in a synergistic quadruple combination of mAbs IgG1b12, 2G12, 2F5, and 4E10 [Xu2001]
- IgG1b12: Oligomeric gp140 (o-gp140) derived from R5 primary isolate US4 was characterized for use as a vaccine reagent – antigen capture ELISA was used to compare the antigenicity of gp120 and o-gp140 using a panel of well characterized MAbs – Abs directed against the CD4 binding site (IgGCD4 and IgG1b12) reacted slightly more strongly with the gp120 monomer than with the oligomer, as did sCD4 [Srivastava2002]
- IgG1b12: The fusion process was slowed by using a suboptimal temperature (31.5 C) to re-evaluate the potential of Abs targeting fusion intermediates to block HIV entry – preincubation of E/T cells at 31.5 C enabled polyclonal anti-N-HR Ab and anti-six-helix bundle Abs to inhibit fusion, indicating six-helix bundles form prior to fusion – the preincubation 31.5 C step did not alter the inhibitory activity of neutralizing Abs anti-gp41 2F5, or anti-gp120 2G12, IG1b12, 48d, and 17b [Golding2002b]
- IgG1b12: Deglycosylation of gp120 does not significantly affect IG1b12 binding, in contrast to MAB 2G12 [Sanders2002]
- IgG1b12: Ab binding characteristics of SOS gp140 were tested using SPR and RIPA – SOS gp140 is gp120-gp41 bound by a disulfide bond – NAbs 2G12, 2F5, IgG1b12, CD4 inducible 17b, and 19b bound to SOS gp140 better than uncleaved gp140 (gp140unc) and gp120 – non-neutralizing MAbs 2.2B (binds to gp41 in gp140unc) and 23A (binds gp120) did not bind SOS gp140 – SOS gp140-2F5-IgG1b12 formed multiple ring structures composed of two SOS gp140 proteins bridged by two Ab molecules, while 2F5 and 2G12 formed extended chains rather than closed rings [Schulke2002]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- IgG1b12: Uncleaved soluble gp140 (YU2 strain, R5 primary isolate) can be stabilized in an oligomer by fusion with a C-term trimeric GCN4 motif or using a T4 trimeric motif derived from T4 bacteriophage fibritin—stabilized oligomer gp140Δ683(-FT) showed strong preferential recognition by NAbs IgG1b12 and 2G12 relative to the gp120 monomer, in contrast to poorly neutralizing MAbs F105, F91, 17b, 48d, and 39F which showed reduced levels of binding, and C11, A32, and 30D which did not bind the stabilized oligomer [Yang2002].
- IgG1b12: The crystal structure of IgG1b12 is resolved and is the first structure of an intact human Ab with an ordered, full length hinge – the structure is extremely asymmetric and flexible with an antigen-binding site that has an unusually long CDR H3 region with a ten residue insertion that projects above the rest of the antigen-binding site – this loop may be required for recognition of the recessed CD4 binding site of gp120 [Saphire2002]‘
- IgG1b12: Alanine scanning mutagenesis used in conjunction with competition and replacement studies of N-linked carbohydrates and sugars suggest that the 2G12 epitope is formed from mannose residues contributed by the glycans attached to N295 and N332, with the other N-linked carbohydrates in positions N339, N386, and N392 playing a role in maintaining conformation relevant to 2G12 binding – N295A and N332A mutants showed essentially unchanged anti-CD4BS NAb b12 binding affinities, while N339A, N386A and N392A mutants displayed significantly lowered b12 affinity, presumably due to conformational changes [Scanlan2002]
- IgG1b12: Passive immunization of neonate macaques with a combination of F105+2G12+2F5 conferred complete protection against oral challenge with SHIV-vpu+ or – the combination b12+2G12+2F5 conferred partial protection against SHIV89.6 – such combinations may be useful for prophylaxis at birth and against milk born transmission – the synergistic combination of IgG1b12, 2G12, 2F5, and 4E10 neutralized a collection of HIV clade C primary isolates [Xu2002]
- IgG1b12: A modified gp140 (gp140ΔCFI), with C-term mutations intended to mimic a fusion intermediate and stabilize trimer formation, retained antigenic conformational determinants as defined by binding to CD4 and to MAbs 2F5, 2G12, F105, and b12, and enhanced humoral immunity without diminishing the CTL response in mice injected with a DNA vaccine [Chakrabarti2002].
- IgG1b12: Called ARP3065: Herpesvirus saimiri-immortalized CD4+ T lymphocytes (HVS T cells) were used to isolate virus and perform HIV-1 neutralization assays, and compared with a standard PBMC protocol – neutralization sensitivities to a panel of MAbs and to homologous or heterologous plasma/sera were similar for HVS T cells (CN-2 cells) and PBMCs [Vella2002]
- IgG1b12: A series of mutational changes were introduced into the YU2 gp120 that favored different conformations – 375 S/W seems to favor a conformation of gp120 closer to the CD4-bound state, and is readily bound by sCD4 and CD4i MAbs (17b, 48d, 49e, 21c and 23e) but binding of anti-CD4BS MAbs (F105, 15e, IgG1b12, 21h and F91 was markedly reduced – IgG1b12 failed to neutralize this mutant, while neutralization by 2G12 was enhanced – 2F5 did not neutralize either WT or mutant, probably due to polymorphism in the YU2 epitope – another mutant, 423 I/P, disrupted the gp120 bridging sheet, favored a different conformation and did not bind CD4, CCR5, or CD4i antibodies, but did bind to CD4BS MAbs [Xiang2002b]
- IgG1b12: Truncation of the gp41 cytoplasmic domain of X4, R5, and X4R5 viruses forces a conformation that more closely resembles the CD4 bound state of the external Envelope, enhancing binding of CD4i MAbs 17b and 48d and of CD4BS MAbs F105, b12, and in most cases of glycosylation site dependent MAb 2G12 and the anti-gp41 MAb 246D – in contrast, binding of the anti-V2 MAb 697D and the anti-V3 MAb 694/98D were not affected – viruses bearing the truncation were more sensitive to neutralization by MAbs 48d, b12, and 2G12 – the anti-C5 MAb 1331A was used to track levels of cell surface expression of the mutated proteins [Edwards2002]
- IgG1b12: Truncation of the gp41 cytoplasmic domain of X4, R5, and X4R5 viruses forces a conformation that more closely resembles the CD4 bound state of the external Envelope, enhancing binding of CD4i MAbs 17b and 48d and of CD4BS MAbs F105, b12, and in most cases of glycosylation site dependent MAb 2G12 and the anti-gp41 MAb 246D – in contrast, binding of the anti-V2 MAb 697D and the anti-V3 MAb 694/98D were not affected – viruses bearing the truncation were more sensitive to neutralization by MAbs 48d, b12, and 2G12 – the anti-C5 MAb 1331A was used to track levels of cell surface expression of the mutated proteins [Edwards2002]
- IgG1b12: HIV-1 gp160ΔCT (cytoplasmic tail-deleted) proteoliposomes (PLs) containing native, trimeric envelope glycoproteins from R5 strains YU2 and JRFL, and X4 strain HXBc2, were made in a physiologic membrane setting as candidate immunogens for HIV vaccines—2F5 bound to gp160ΔCT with a reconstituted membrane ten-fold better than the same protein on beads—anti-CD4BS MAbs IgG1b12 and F105, A32 (C1-C4), C11 (C1-C5), and 39F (V3) MAbs bound gp160ΔCT PLs indistinguishably from gp160ΔCT expressed on the cell surface—non-neutralizing MAbs C11 and A32 bound with lower affinity than NAb IgG1b12—the MAb 17b was sCD4 inducible on gp160ΔCT PL [Grundner2002].

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- IgG1b12: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain [Zhang2002]
- IgG1b12: A broad review of NAbs that mentions IgG1b12 as an example of a NAb that does not alter the conformation of gp120, but interferes with CD4 binding [Klasse2002]
- IgG1b12: Review of NAbs that notes IgG1b12 is a recombinant IgG1 from a phage displayed Fab generated against gp120 from a B clade infected individual, that it binds the CD4BS, that alone or in combination with other MAbs it can protect some macaques against SHIV infection, and that it has strong ADCC activity [Ferrantelli2002]‘
- IgG1b12: Review of NAbs that discusses mechanisms of neutralization, passive transfer of NAbs and protection in animal studies, and vaccine strategies [Liu2002]
- IgG1b12: Virion capture assays are not a good preditor of neutralization, and the presentation of epitopes using this assay seems to be different from that of functional Envelope spikes on primary isolates – F105 and b6 could efficiently block the b12-mediated capture of infectious virions in a virus capture, but did not inhibit b12 neutralization – b12 was potent at neutralizing the three primary virions JR-CSF, ADA, and 89.6, but anti-V3 Abs 447-52D and 19b, which did not neutralize JR-CSF and ADA captured amounts of p24 equal to or higher than the amounts captured by the neutralizing Ab b12 [Poignard2003]
- IgG1b12: Called b12 – Alanine scanning mutagenesis was used to compare substitutions that affected anti-CD4BS NAb b12 binding to those that affect binding of sCD4 and two non-neutralizing anti-CD4BS Abs b3 and b6 – while the epitope maps overlapped, there were some differences observed – binding of CD4 was never in enhanced, indicating it had evolved to be optimal – rec gp120s were engineered to contain combinations of Alanine substitutions that enhanced b12 binding, and while binding of b12 to these gp120 monomers was generally maintained or increased, binding by five non-neutralizing anti-CD4bs MAbs (b3, b6, F105, 15e, and F91) was reduced or completely abolished – 2G12 binding was largely unperturbed, indicating these proteins were not grossly misfolded – for twelve mutants, b12 neutralization sensitivity and affinity correlated, but for five mutants neutralization efficiency was maintained or increased despite a decrease in affinity [Pantophlet2003]
- IgG1b12: Called b12 – CD4BS MAbs b12 (neutralizing) and 205-42-15, 204-43-1, 205-46-9 (nonneutralizing) all cross-competed for binding to monomeric gp120, indicating the topological proximity of their epitopes, however, the nonneutralizing CD4BS MAbs did not interfere with the neutralization activity of MAb b12 – the nonneutralizing MAbs partially competed with b12 for Env binding of the surface of Env-transfected cells – this suggests Env has two categories of binding site for CD4BS MAbs, one recognized by both b12 and nonneutralizing CD4BS MAbs, the other is recognized by only b12 – Ab-gp120 interactions based on the use of monomeric gp120 or Env-transfected cells do not predict the outcome of HIV-1 neutralization assays, and they should be interpreted with caution [Herrera2003]
- IgG1b12: UK Medical Research Council AIDS reagent: ARP3065
- IgG1b12: NIH AIDS Research and Reference Reagent Program: 2640

935	IgGCD4 (IgG-CD4)	Env	gp120				human (IgG)

Ab type CD4BS

References Capon1989, Stamatatos1998, Ly2000, Srivastava2002

- IgGCD4: An antibody-like immunoadhesins molecule was constructed incorporating the gp120-binding domain of CD4 [Capon1989]
- IgGCD4: Deleting the V2 loop of neutralization-resistant HIV-1 isolate SF162 does not abrogate its replication in PBMC or macrophages, but it enhances its neutralization sensitivity to sera from patients with B clade infection up to 170-fold, and also enhances sensitivity to sera from clades A through F – deletion of V2 but not V1 slightly enhanced neutralization by CD4BS MAb IgGCD4 [Stamatatos1998]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• IgGCD4: SF162 is a neutralization-resistant HIV-1 isolate – N-linked glycosylation modifications in the V2 loop of the SF162 gp120 revealed that these sites prevent neutralization by CD4BS MAbs (IgG1b12 and IgGCD4), and protect against neutralization by V3 MAbs (447-D and 391-95D) – V2-region glycosylation site mutations did not alter neutralization resistance to V2 MAbs (G3.4 and G3.136) or CD4i MAbs (17b and 48d) – V2 glycosylation site modification allows infection of macrophages, probably due to glycosylated forms requiring fewer CCR5 molecules for viral entry [Ly2000] • IgGCD4: Oligomeric gp140 (o-gp140) derived from R5 primary isolate US4 was characterized for use as a vaccine reagent – antigen capture ELISA was used to compare the antigenicity of gp120 and o-gp140 using a panel of well characterized MAbs – Abs directed against the CD4 binding site (IgGCD4 and IgG1b12) reacted slightly more strongly with the gp120 monomer than with the oligomer, as did sCD4 [Srivastava2002]				
936	L28	Env	gp120		L	HIV-1 infection	human (IgG1κ)
		Ab type CD4BS **References** Ditzel1995 • L28: Substitutions at 257 T/R, 368 D/R, 370 E/R and 370 E/Q, 475 M/S 102 E/L and 463 N/D reduce binding – binding was enhanced by removal of the V3 loop and by substitutions 45 W/S, 298 R/G, 381 E/P, 382 F/L, 420 I/R, 435 Y/H or Y/R – binding is sensitive to deglycosylation – heavy and light chain variable region sequence is available [Ditzel1995]					
937	L33	Env	gp120		L	HIV-1 infection	human (IgG1κ)
		Ab type CD4BS **References** Ditzel1995 • L33: binding is sensitive to deglycosylation – heavy and light chain variable region sequence is available [Ditzel1995]					
938	L41	Env	gp120		L	HIV-1 infection	human (IgG1κ)
		Ab type CD4BS **References** Ditzel1995 • L41: Substitutions at 133 D/R, 256 S/Y, 257 T/R, 368 D/R or D/T, 370 E/Q or E/R, 384 Y/E, and 421 K/L reduce binding – paradoxically, this Fab was retrieved from the library after masking with known anti-CD4BS MAbs – binding is sensitive to deglycosylation – heavy and light chain variable region sequence is available [Ditzel1995]					
939	L42	Env	gp120		L	HIV-1 infection	human (IgG1κ)
		Ab type CD4BS **References** Ditzel1995 • L42: Substitutions at 257 T/R, 368 D/R, 370 E/R, 266 A/E and 477 D/V reduce binding – binding was significantly enhanced by 381 E/P and 382 F/L – binding is sensitive to deglycosylation – heavy and light chain variable region sequence is available [Ditzel1995]					
940	L52	Env	gp120		L	HIV-1 infection	human (IgG1κ)
		Ab type CD4BS **References** Ditzel1995 • L52: Binding is sensitive to deglycosylation – heavy and light chain variable region sequence is available [Ditzel1995]					
941	L72	Env	gp120				murine
		Ab type CD4BS **Donor** Dr. Hariharam, IDEC Pharmaceuticals Corp La Jolla, CA **References** Ditzel1997 • L72: Used to bind gp120 to solid phase to select MAbs from a phage selection library [Ditzel1997]					
942	M12	Env	gp120 (IIIB)		L	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		Ab type CD4BS **Donor** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD **References** Earl1994, Sugiura1999 • M12: There is a p15 gag specific MAb also named M12 • M12: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response [Earl1994] • M12: A comparison of 25 gp120 specific, conformation dependent MAbs was done – M12 is part of a group of MAbs labeled A1 – all A1 MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, blocked CD4 binding, were sensitive to mutations in gp120 positions 368 and 370 that directly contact CD4 – 50% neutralization of NL4-3 was achieved with 21 ug/ml of M12 [Sugiura1999]				
943	M13	Env	gp120 (IIIB)		L	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140 **Ab type** CD4BS **Donor** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD **References** Earl1994, Sugiura1999 • M13: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response [Earl1994] • M13: A comparison of 25 gp120 specific, conformation dependent MAbs was done – M13 is part of a group of MAbs labeled A1 – all A1 MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, blocked CD4 binding, were sensitive to mutations in gp120 positions 368 and 370 that directly contact CD4 – 50% neutralization of NL4-3 was achieved with 35 ug/ml of M13 [Sugiura1999]				
944	M6	Env	gp120 (IIIB)		no	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140 **Ab type** CD4BS **Donor** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD **References** Earl1994, Sugiura1999 • M6: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response [Earl1994] • M6: A comparison of 25 gp120 specific, conformation dependent MAbs was done – M6 is part of a group of MAbs labeled A1 – all A1 MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, blocked CD4 binding, were sensitive to mutations in gp120 positions 368 and 370 that directly contact CD4 [Sugiura1999]				
945	MAG 116	Env	gp120		L	Vaccine	murine
		Vaccine *Vector/Type:* sCD4-gp120 complex *Strain:* HXB2 *HIV component:* gp120 **Ab type** CD4BS **Donor** C. Y. Kang, IDEC Inc **References** Kang1994 • MAG 116: Amino acid substitutions that reduce binding 10 fold: 256 S/Y, 257 T/R, 368 D/R or T, 370 E/R or Q, 384 Y/E, 421 K/L – neutralizes MN, IIIB and RF [Kang1994]				
946	MAG 12B	Env	gp120		L	Vaccine	murine
		Vaccine *Vector/Type:* sCD4-gp120 complex *Strain:* HXB2 *HIV component:* gp120 **Ab type** CD4BS **Donor** C. Y. Kang, IDEC Inc **References** Kang1994 • MAG 12B: Amino acid substitutions that reduce binding 10 fold: 257 T/R, 368 D/R or T, 370 E/R or Q, 384 Y/E, 477 D/V – weak neutralization of IIIB [Kang1994]				
947	MAG 29B	Env	gp120		L	Vaccine	murine
		Vaccine *Vector/Type:* sCD4-gp120 complex *Strain:* HXB2 *HIV component:* gp120 **Ab type** CD4BS **Donor** C. Y. Kang, IDEC Inc **References** Kang1994				

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• MAG 29B: Amino acid substitutions that reduce binding 10 fold: 257 T/R, 368 D/R or T, 370 E/R or Q, 384 Y/E, 386 N/Q, 421 K/L – weak neutralization of IIIB [Kang1994]					
948	MAG 3B	Env	gp120		no	Vaccine	murine
		Vaccine *Vector/Type:* sCD4-gp120 complex *Strain:* HXB2 *HIV component:* gp120 **Ab type** CD4BS **Donor** C. Y. Kang, IDEC Inc **References** Kang1994 • MAG 3B: Amino acid substitutions that reduce binding 10 fold: 256 S/Y, 257 T/R or A or G, 262 N/T, 368 D/R or T, 370 E/R or Q, 381 E/P, 384 Y/E, 421 K/L, 475 M/S, 477 D/V [Kang1994]					
949	MAG 55 (#55)	Env	gp120		L	Vaccine	murine
		Vaccine *Vector/Type:* sCD4-gp120 complex *Strain:* HXB2 *HIV component:* gp120 **Ab type** CD4BS **Donor** C. Y. Kang, IDEC Inc **References** Kang1994, Moore1996 • MAG 55: Amino acid substitutions that reduce binding 10 fold: 256 S/Y, 257 T/R, 368 D/R or T, 370 E/R or Q, 384 Y/E, 421 K/L, 470 P/L, 475 M/S, 477 D/V – neutralizes MN, IIIB and RF [Kang1994] • MAG 55: Called #55 – binding reciprocally inhibited by other anti-CD4 binding site MAbs, and by some C1-C5 MAbs – binding enhanced by anti-V3 MAb 110.5 and anti-V2 MAbs G3-136 and G3-4 – enhances binding of many anti-V3 and -V2 MAbs. [Moore1996]					
950	MAG 72 (L72)	Env	gp120		L	Vaccine	murine
		Vaccine *Vector/Type:* sCD4-gp120 complex *Strain:* HXB2 *HIV component:* gp120 **Ab type** CD4BS **Donor** C. Y. Kang or Dr. Hariharam, IDEC Pharmaceuticals Corp, La Jolla, CA **References** Kang1994, Ditzel1997 • MAG 72: Amino acid substitutions that reduce binding 10 fold: 257 T/R or A or G, 262 N/T, 368 D/R or T, 370 E/R or Q, 384 Y/E, 421 K/L, 477 D/V – neutralizes MN, IIIB and RF [Kang1994] • MAG 72: Called L72 – used to bind gp120 to solid phase to select MAbs from a phage selection library [Ditzel1997]					
951	MAG 86	Env	gp120		L	Vaccine	murine
		Vaccine *Vector/Type:* sCD4-gp120 complex *Strain:* HXB2 *HIV component:* gp120 **Ab type** CD4BS **Donor** C. Y. Kang, IDEC Inc **References** Kang1994 • MAG 86: Amino acid substitutions that reduce binding 10 fold: 256 S/Y, 257 T/R, 368 D/R or T, 370 E/R or Q, 384 Y/E, 421 K/L, 470 P/L, 477 D/V – neutralizes MN, IIIB and RF [Kang1994]					
952	MAG 96	Env	gp120		L	Vaccine	murine
		Vaccine *Vector/Type:* sCD4-gp120 complex *Strain:* HXB2 *HIV component:* gp120 **Ab type** CD4BS **Donor** C. Y. Kang, IDEC Inc **References** Kang1994 • MAG 96: Amino acid substitutions that reduce binding 10 fold: 256 S/Y, 257 T/R, 368 D/R or T, 370 E/R – weak neutralization of IIIB [Kang1994]					
953	MTW61D	Env	gp120 (W61D)		L	HIV-1 infection	human
		Ab type CD4BS **References** Sullivan1998a					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• MTW61D – the HIV-1 virus YU2 entry can be enhanced by MAbs binding to the CD4BS, V3 loop, and CD4i epitopes – the activation for this enhanced entry state could be conferred on HxB2 by introducing the YU2 V3 loop, or the YU2 V3 and V1/V2 loops – a similar effect is observed by sub-neutralizing concentrations of sCD4 and the effect is dependent of CCR5 – Fab fragment MTW61D also enhances YU2 entry, ruling out Fc interactions or Env cross-linking as a mechanism, while neutralizing HXBc2 – MTW61D was obtained by panning libraries derived from bone marrow from a long term asymptomatic donor against gp120 from primary isolate W61D [Sullivan1998a]					
954	S1-1	Env	gp120		L	HIV-1 infection	human (IgG1λ)
		Ab type CD4BS **References** Lake1992, Moran1993, Wisnewski1996 • S1-1: Neutralizes IIIB and MN without complement, and neutralizes RF and a clinical isolate with complement – binds to native but not denatured gp120 – inhibits sCD4-gp120 binding [Lake1992] • S1-1: Heavy (V HI) and light (V lambdaIII) chain sequenced – no enhancing activity – similar germline sequence to MAb 86, but very different activity [Moran1993] • S1-1: S1-1 is V H1 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals [Wisnewski1996]					
955	T13	Env	gp120 (IIIB)		no	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140 **Ab type** CD4BS **Donor** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD **References** Earl1994, Sugiura1999 • T13: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response [Earl1994] • T13: A comparison of 25 gp120 specific, conformation dependent MAbs was done – T13 is one of three MAbs labeled group Cb, that was type-specific for BH8 – T13 fully blocked CD4 binding, and the deletion of the V3 loop enhanced binding 10-fold [Sugiura1999]					
956	T49	Env	gp120 (IIIB)		no	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140 **Ab type** CD4BS **Donor** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD **References** Earl1994, Sugiura1999 • T49: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response [Earl1994] • T49: A comparison of 25 gp120 specific, conformation dependent MAbs was done – T49 is one of three MAbs labeled group Cb, that was type-specific for BH8 – T49 fully blocked CD4 binding, and the deletion of the V3 loop enhanced binding 10-fold [Sugiura1999]					
957	T56	Env	gp120 (IIIB)		no	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140 **Ab type** CD4BS **Donor** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD **References** Earl1994, Sugiura1999 • T56: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response [Earl1994] • T56: A comparison of 25 gp120 specific, conformation dependent MAbs was done – T56 is one of three MAbs labeled group Cb, that was type-specific for BH8 – T56 fully blocked CD4 binding, and the deletion of the V3 loop enhanced binding 10-fold [Sugiura1999]					
958	TH9	Env	gp120		L		human (IgG1κ)
		Ab type CD4BS **Donor** Michael Fung, Tanox Biosystem, USA **References** D'Souza1995, Yang1998					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• TH9: Found to neutralize MN, but not JRCSF, two B subtype primary isolates, or a D subtype primary isolate, by most labs in a multi-laboratory study involving 11 labs[D'Souza1995] • TH9: A neutralization assay was developed based on hemi-nested PCR amplification of the LTR (HNPCR) – LTR-HNPCR consistently revealed HIV DNA and was shown to be a rapid, specific and reliable neutralization assay based on tests with 6 MAbs and 5 isolates [Yang1998]					
959	anti-CD4BS summary	Env	gp120				
		Ab type CD4BS **References** Thali1993, Moore1996 • Shared components of MAb epitopes and the discontinuous CD4 binding regions included Thr 257, Asp 368, Glu 370, Lys 421 through Trp 427 and Asp 457 [Thali1993] • Anti-CD4 binding site antibodies (CD4BS) competitively inhibit CD4 binding to monomeric gp120, and they differ in precise dependence on gp120 residues, but generally require Asp-368 and Glu-370 [Moore1996]					
960	b11	Env	gp120				human
		Ab type CD4BS **References** Parren1998a • b11: The rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142-10 > DA48 > L17) was markedly different than Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142-10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren1998a]					
961	b13	Env	gp120				human
		Ab type CD4BS **References** Parren1995, Parren1998a, Parren1997a • b13: Fab b13 was used as a control in a hu-PBL SCID mouse study – animals were protected from HIV-1 SF2 infection by IgG1b12, somewhat by Fab b12, but not by b13 [Parren1995, Parren1997a] • b13: The rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142-10 > DA48 > L17) was markedly different than Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142-10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren1998a]					
962	b14	Env	gp120				human
		Ab type CD4BS **References** Parren1998a • b14: The rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142-10 > DA48 > L17) was markedly different than Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142-10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren1998a]					
963	b3	Env	gp120				human
		Ab type CD4BS **References** Parren1997c, Parren1998a, Pantophlet2003 • b3: Neutralizes TCLA strains, but not primary isolates [Parren1997c]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- b3: The rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142-10 > DA48 > L17) was markedly different than Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142-10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren1998a]
- b3: Alanine scanning mutagenesis was used to compare substitutions that affected anti-CD4BS NAb b12 binding to those that affect binding of sCD4 and two non-neutralizing anti-CD4BS Abs b3 and b6 – while the epitope maps overlapped, there were some differences observed – binding of CD4 was never in enhanced, indicating it had evolved to be optimal – rec gp120s were engineered to contain combinations of Alanine substitutions that enhanced b12 binding, and while binding of b12 to these gp120 monomers was generally maintained or increased, binding by five non-neutralizing anti-CD4bs MAbs (b3, b6, F105, 15e, and F91) was reduced or completely abolished – 2G12 binding was largely unperturbed, indicating these proteins were not grossly misfolded [Pantophlet2003]

964 b6 Env gp120 L human

Ab type CD4BS **Donor** Dennis Burton, Scripps, San Diego, CA, USA
References Parren1997c, Parren1998a, Poignard2003, Pantophlet2003

- b6: Neutralizes TCLA strains, but not primary isolates [Parren1997c]
- b6: The rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142-10 > DA48 > L17) was markedly different than Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142-10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren1998a]
- b6: Virion capture assays are not a good preditor of neutralization, and the presentation of epitopes using this assay seems to be different from that of functional Envelope spikes on primary isolates – F105 and b6 could efficiently block the b12-mediated capture of infectious virions in a virus capture, but did not inhibit b12 neutralization – while b12 was potent at neutralizing the three primary virions JR-CSF, ADA, and 89.6, the Abs F105, 19b, and Fab b6 were overall very poor neutralizers [Poignard2003]
- b6: Alanine scanning mutagenesis was used to compare substitutions that affected anti-CD4BS NAb b12 binding to those that affect binding of sCD4 and two non-neutralizing anti-CD4BS Abs b3 and b6 – while the epitope maps overlapped, there were some differences observed – binding of CD4 was never in enhanced, indicating it had evolved to be optimal – rec gp120s were engineered to contain combinations of Alanine substitutions that enhanced b12 binding, and while binding of b12 to these gp120 monomers was generally maintained or increased, binding by five non-neutralizing anti-CD4bs MAbs (b3, b6, F105, 15e, and F91) was reduced or completely abolished – 2G12 binding was largely unperturbed, indicating these proteins were not grossly misfolded [Pantophlet2003]

965 polyclonal Env gp120 no Vaccine murine

Vaccine *Vector/Type:* recombinant protein, virus-like particle *Strain:* LAI *HIV component:* V3, CD4BS, p55
Ab type CD4BS
References Truong1996

- Antibodies raised against recombinant anti-p55 virus-like particles with the p24 region 196-226 deleted, bearing inserts of either the V3 or the CD4BS regions of gp120 were studied – no neutralizing responses, weak Env and strong Gag responses were elicited – the major homology region (MHR) and proximal sequences was found to be required for capsid assembly [Truong1996]

966 D33 Env gp120 (IIIB) Vaccine murine (IgG)

Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140
Ab type CD4BS, C-term, N-term **Donor** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References Earl1994, Sugiura1999

- D33: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response [Earl1994]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- D33: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D33 is part of a group of MAbs labeled A1 – all A1 MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, blocked CD4 binding, were sensitive to mutations in gp120 positions 368 and 370 that directly contact CD4 – D33 was unusual for the group of A1 MAbs, because while it blocked CD4 binding completely, but competed with MAbs that did not in a BIAcore assay – both the N- and C-terminal ends of gp120 are involved in D33 binding [Sugiura1999]

967 Env gp120 yes human

Ab type CD4BS, CD4i, V3, V2

References Moore2001

- Moore and colleagues review structural aspects of gp120 and how they relate to antigenic domains, and review the data concerning the lack of a clear relationship between genetic subtype and serotype – they suggest the primary goal in vaccine efforts should be to design an immunogen that can be shown to elicit neutralizing antibodies against a significant proportion of primary isolates – assay artifacts that can result in confused interpretations are also discussed, such as Ab binding to defective spikes, which does not affect HIV-1 infectivity, but can dominant an assay signal [Moore2001]

968 17b Env gp120 L P (weak) HIV-1 infection human

Ab type CD4i **Donor** James Robinson, Tulane University, New Orleans, LA, USA

References

Thali1993, Moore1993d, Thali1994, Beretta1994, Wyatt1995, Sattentau1995b, Moore1996, Poignard1996a, Wu1996, Trkola1996a, Binley1997a, Fouts1997, Li1997, Weinberg1997, Ditzel1997, Cao1997b, Wyatt1997, Parren1997c, Kwong1998, Wyatt1998a, Moore1998, Rizzuto1998, Sullivan1998b, Sullivan1998a, Binley1998, Stamatatos1998, Oscherwitz1999a, Hoffman1999, Binley1999, Grovit-Ferbas2000, Ly2000, Park2000, Salzwedel2000, Stamatatos2000, Yang2000, Rizzuto2000, Si2001, Kolchinsky2001, York2001, Zhang2001a, Poignard2001, Srivastava2002, Golding2002b, Schulke2002, Yang2002, Dowd2002, Xiang2002b, Xiang2002a, Edwards2002, Grundner2002, Basmaciogullari2002, Zhang2002, Arthos2002

- 17b: 48d and 17b have similar epitopes, and the pair are unique among human and rodent MAbs
- 17b: Epitope is better exposed upon CD4 binding to gp120 – competes with 15e and 21h, anti-CD4 binding site MAbs – 113 D/R, 252 R/W, 257 T/A or G, 370 E/D, 382 F/L, 420 I/R, 433A/L, 438 P/R and 475 M/S confer decreased sensitivity to neutralization [Thali1993]
- 17b: Binding of 48d is much more influenced by sequence variation among molecular clones of LAI than is binding of 17b [Moore1993d]
- 17b: A mutation in gp41, 582 A/T, confers resistance to neutralization (also confers resistance to MAbs F105, 48d, 21h and 15e) [Thali1994]
- 17b: Studies using a V1/V2 deletion mutant demonstrated that enhanced binding of 17b in the presence sCD4 involves the V1/V2 loops, with more significant involvement of V2 – similar effect observed for 48d and A32 [Wyatt1995]
- 17b: Binds with higher affinity to monomer and oligomer, slow association rate, poor neutralization of lab strain – this is in contrast to 48d, which has very different kinetics [Sattentau1995b]
- 17b: Many MAbs inhibit binding (anti-C1, -C5, -C4, -CD4BS) – anti-V3 MAb 5G11 enhances binding, as do C1-C4 discontinuous epitopes A32 and 2/11c – enhances binding of some anti-V2 MAbs [Moore1996]
- 17b: Binding did not result in significant gp120 dissociation from virion, in contrast to 48d, although the gp41 epitope of MAb 50-69 was exposed [Poignard1996a]
- 17b: MIP-1α binding to CCR-5 expressing cells can be inhibited by gp120-sCD4 — binding of 17b blocks this inhibition [Wu1996].
- 17b: Neutralizes JR-FL – inhibits gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study [Trkola1996a]
- 17b: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric Env binding – 17b bound monomer, oligomer, and neutralized JRFL in the presence of sCD4, but if sCD4 was not present, 17b only bound monomer [Fouts1997]
- 17b: One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB env – 17b has synergistic response in combination with anti-V3 MAb 694/98-D [Li1997]
- 17b: 48d binds to the IIIB protein and not IIIB V3 peptide, while binding to the Can0A V3 peptide, suggesting Can0A V3 is a conformer that mimics the 48d – it does not bind to 17b, distinguishing the epitopes [Weinberg1997]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 17b: Virus with the V1-V2 loop deleted was viable and more susceptible to neutralization by CD4i MAb 17b, and anti-V3 MAbs 1121, 9284, and 110.4, but not to a CD4BS MAb, F105, or sCD4 [Cao1997b]
- 17b: Binds to sgp120 efficiently, but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding – partial re-exposure if sCD4 was bound – could not bind to HXBc2 gp120 if the 19 C-term amino acids were deleted in conjunction with amino acids 31-93 in C1, but binding was restored in the presence of sCD4 [Wyatt1997]
- 17b: Neutralizes TCLA strains, but not primary isolates [Parren1997c]
- 17b: 17b Fab was co-crystallized with a gp120 core and CD4, and it's binding site can be directly visualized—17b binds to the "bridging sheet" of gp120, an antiparallel beta sheet region, contacting residues from the C4 region and the V1/V2 stem—the contact area is small for an Ab-antigen interactive surface, and dominated in the Ab by the heavy chain—the center of the binding region has hydrophobic interactions, and the periphery charge interactions, acidic on 17b and basic on gp120 [Kwong1998]
- 17b: Summary of the implications of the crystal structure of a gp120 core bound to CD4 and 17b, combined with what is known about mutations that reduce NAb binding to gp120 – probable mechanism of neutralization is interference with chemokine receptor binding – mutations in 88N, 117K, 121K, 256S, 257T, N262, Delta V3, E370, E381, F 382, R 419, I 420, K 421, Q 422, I 423, W 427, Y 435, P 438, M 475 of HXBc2 (IIIB) reduce binding – the only variable residues in gp120 that contact 17b are 202T and 434M – the contact points for 17b with the crystallized incomplete gp120 are mostly in the heavy chain of the Ab, and there is a gap between 17b's light chain and the partial gp120 which may be occupied by the V3 loop in a complete gp120 molecule – the authors propose that the V2 and V3 loops may mask the CD4i Ab binding site, and that the V2 loop may be repositioned upon CD4 binding [Wyatt1998a]
- 17b: Moore and Binley provide a commentary on the papers by [Rizzuto1998], [Wyatt1998a] and [Kwong1998] – they point out 17b shares binding elements in gp120 with chemokine receptor molecules, and that CD4 needs to bind to gp120 first to make the 17b epitope accessible and it may be sterically blocked in the CD4 bound virus, thus making it a poor NAb for primary isolates [Moore1998]
- 17b: Site directed mutagenesis of a WU2 protein with the V1-V2 loops deleted revealed key residues for 17b-gp120 interaction and interaction of gp120 and CCR5 – mutations in residues that reduced 17b by 70% were R/D 419, I/R 420, Q/L 422, Y/S 435, I/S 423, K/D 121 and K/D 421– 17b can neutralize HIV-1 strains that use different chemokine receptors, supporting a common region in gp120 in chemokine-receptor interaction [Rizzuto1998]
- 17b: sCD4 induces 17b binding in primary isolates and TCLA strains – amino acids that reduce the efficiency of binding were determined and found also to compromise syncytia formation and viral entry – V1V2 deletion or sCD4 binding can expose the 17b epitope for both HXBc2 and macrophage tropic YU2 – neutralizing potency of 17b is probably weak due to poor exposure of the epitope – 17b epitope exposure upon sCD4 binding can occur over a wide range of temperatures, consistent with the energy of CD4 binding being sufficient to drive the V1/V2 loop into a new conformation [Sullivan1998b]
- 17b: The HIV-1 virus YU2 entry can be enhanced by MAbs binding to the CD4BS, V3 loop, and CD4i epitopes – the activation for this enhanced entry state could be conferred on HxB2 by introducing the YU2 V3 loop, or the YU2 V3 and V1/V2 loops, and the presence of V1/V2 increased the enhancement – a similar effect is observed by sub-neutralizing concentrations of sCD4 and the effect is dependent of CCR5 – 17b enhances YU2 enhanced viral entry 10-fold, whereas HXBc2 was neutralized [Sullivan1998a]
- 17b: A panel of MAbs was shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer – CD4i MAbs 17b and 48d bound better to the deleted protein than to wild type [Binley1998]
- 17b: Deleting the V2 loop of neutralization-resistant HIV-1 isolate SF162 does not abrogate its replication in PBMC or macrophages, but it enhances its neutralization sensitivity to sera from patients with B clade infection up to 170-fold, and also enhances sensitivity to sera from clades A through F – deletion of V2 but not V1 enabled neutralization by CD4i MAbs 17b and 48d [Stamatatos1998]
- 17b: A CD4-independent viral variant of IIIB, IIIBx, was generated on CXCR4-expressing cells – IIIBx exhibited greater exposure of the 17b and 48d epitopes and enhanced neutralization by CD4i MAbs and by polyclonal human sera – the 17b epitope has significant overlap with the CCR5 coreceptor binding site [Hoffman1999]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 17b: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes [Binley1999]
- 17b: To determine the antigenicity of virus killed by thermal and chemical inactivation, retention of conformation-dependent neutralization epitopes was examined, and exposure of CD4BS epitopes was found to be enhanced (MAbs IgG1b12, 205-46-9, and 205-43-1) – binding to 2G12 and 447-52D epitopes was essentially unaltered – the 17b CD4i epitope was also exposed [Grovit-Ferbas2000]
- 17b: SF162 is a neutralization-resistant HIV-1 isolate – N-linked glycosylation modifications in the V2 loop of the SF162 gp120 revealed that these sites prevent neutralization by CD4BS MAbs (IgG1b12 and IgGCD4), and protect against neutralization by V3 MAbs (447-D and 391-95D) – V2-region glycosylation site mutations did not alter neutralization resistance to V2 MAbs (G3.4 and G3.136) or CD4i MAbs (17b and 48d) – V2 glycosylation site modification allows infection of macrophages, probably due to glycosylated forms requiring fewer CCR5 molecules for viral entry [Ly2000]
- 17b: Six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20-100 fold more efficient at neutralizing the sensitive form – the mutation L544P reduced binding of all MAbs against gp120 by causing conformational changes [Park2000]
- 17b: sCD4 can activate fusion between effector cells expressing Env and target cells expressing coreceptor (CCR5 or CXCR4) alone without CD4 – CD4i MAbs 17b and 48d have little effect on a standard cell fusion assay but potently block sCD4 activated fusion – 17b was broadly cross-reactive inhibiting sCD4 activated fusion with Env from clades A, B, C, D, E, F, and F/B [Salzwedel2000]
- 17b: Soluble gp140 derived from SF162, a neutralization-resistant primary isolate, and SF162AV2 a neutralization-susceptible isolate with 30 amino acids deleted from the V2 loop, were generated with or without the gp120-gp41 cleavage site intact – all forms are recognized by oligomer-specific MAb T4 and show enhanced binding of CD4i MAb 17b when sCD4 is bound – the fused forms are less efficiently recognized than the cleaved forms by polyclonal neutralizing sera from HIV-infected patients – the V3 loop is more exposed on the fused form [Stamatatos2000]
- 17b: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) that preserve and expose some neutralizing epitopes while occluding some non-neutralizing epitopes – CD4BS MAbs (F105 and F91) and CD4i (17b and 48d) recognized gp140-GNC4 as well as gp120 or gp140 – non-neutralizing MAbs C11, A32, 522-149, M90, and #45 bound to the gp140-GNC4 glycoprotein at reduced levels compared to gp120 – MAbs directed at the extreme termini of gp120 C1 (135/9 and 133/290) and C5 (CRA-1 and M91) bound efficiently to gp140-GNC4 [Yang2000]
- 17b: Mutagenesis defines Ile-420, Lys-421, Gln-422, Pro-438, and Gly-441 to be important residues for CCR5 binding – these positions are located on two strands that connect the gp120 bridging sheet and outer domain, suggesting a mechanism for conformational shifts induced by CD4 binding to facilitate CCR5 binding [Rizzuto2000]
- SHIV-HXBc2 is a neutralization sensitive non-pathogenic virus, and several in vivo passages through monkey's yielded highly pathogenic SHIV KU-1 – HXBc2 and the KU-1 clone HXBc2P3.2 differ in 12 amino acids in gp160 – substitutions in both gp120 and gp41 reduced the ability of sCD4, IgG1b12, F105 and AG1121 to Env achieve saturation and full occupancy, and neutralize KU-1 – 17b and 2F5 also bound less efficiently to HXBc2P3.2, although 2G12 was able to bind both comparably [Si2001]
- 17b: Mutations in two glycosylation sites in the V2 region of HIV-1 ADA at positions 190 and 197 (187 DNTSYRLINCNTS 199) cause the virus to become CD4-independent and able to enter cells through CCR5 alone—these same mutations tended to increase the neutralization sensitivity of the virus, including to 17b—only the CD4i antibodies 17b and 48d showed an increased affinity of the CD4 independent viruses relative to wild-type [Kolchinsky2001].

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 17b: Abs against the V3 loop (50.1, 58.2, 59.1, 257-D, 268-D, 447-52D), CD4BS (IgG1b12, 559-64D, F105), CD4i (17b), and to gp41 (2F5, F240) each showed similar binding efficiency to Env derived from related pairs of primary and TCLA lines (primary: 168P and 320SI, and TCLA: 168C and 320SI-C3.3), but the TCLA lines were much more susceptible to neutralization suggesting that the change in TCLA lines that make them more susceptible to NAbs alters some step after binding – 17b bound at somewhat greater levels to 168C than to 168P, but this is not a general feature of 17b binding to primary versus TCLA strains [York2001]
- 17b: 17b binds to a CD4 inducible epitope which partially overlaps the CCR5 binding site – JRFL, YU2, 89.6, and HXB2 and their C1-, V1/V2-, C5 -deletion mutants were used to study how 17b binding affects gp120-CD4 interactions – 17b reduced CD4-gp120 interactions by decreasing the on-rate and increasing the off-rate of sCD4, while enhanced binding of sCD4 binding was observed for the 17b-bound, V1/V2 deleted gp120s – 17b was considered to be a surrogate for CCR5, and the authors suggest that 17b binding may shift V1/V2 into a position that interferes with CD4 binding, forcing a release [Zhang2001a]
- 17b: Structural aspects of the interaction of neutralizing Abs with HIV-1 Env are reviewed – Env essentially has three faces, one is largely inaccessible on the native trimer, and two that exposed but have low immunogenicity on primary viruses – neutralization is suggested to occur by inhibition of the interaction between gp120 and the target cell membrane receptors as a result of steric hindrance and it is noted that the attachment of approximately 70 IgG molecules per virion is required for neutralization, which is equivalent to about one IgG molecule per spike – the 2G12, 17b and b12 epitopes are discussed in detail – the 17b epitope is masked prior to CD4 binding by the V1-V2 loop and in contrast to sCD4, the binding of cell surface CD4 to virus does not appear to make the epitope accessible to binding by 17b to allow neutralization [Poignard2001]
- 17b: Oligomeric gp140 (o-gp140) derived from R5 primary isolate US4 was characterized for use as a vaccine reagent – antigen capture ELISA was used to compare the antigenicity of gp120 and o-gp140 using a panel of well characterized MAbs – 17b recognized both gp120 monomer and o-gp140 [Srivastava2002]
- 17b: The fusion process was slowed by using a suboptimal temperature (31.5 C) to re-evaluate the potential of Abs targeting fusion intermediates to block HIV entry – preincubation of E/T cells at 31.5 C enabled polyclonal anti-N-HR Ab and anti-six-helix bundle Abs to inhibit fusion, indicating six-helix bundles form prior to fusion – the preincubation 31.5 C step did not alter the inhibitory activity of neutralizing Abs anti-gp41 2F5, or anti-gp120 2G12, IG1b12, 48d, and 17b [Golding2002b]
- 17b: Ab binding characteristics of SOS gp140 were tested using SPR and RIPA – SOS gp140 is gp120-gp41 bound by a disulfide bond – NAbs 2G12, 2F5, IgG1b12, CD4 inducible 17b, and 19b bound to SOS gp140 better than uncleaved gp140 (gp140unc) and gp120 – non-neutralizing MAbs 2.2B (binds to gp41 in gp140unc) and 23A (binds gp120) did not bind SOS gp140 [Schulke2002]
- 17b: Uncleaved soluble gp140 (YU2 strain, R5 primary isolate) can be stabilized in an oligomer by fusion with a C-term trimeric GCN4 motif or using a T4 trimeric motif derived from T4 bacteriophage fibritin—stabilized oligomer gp140Δ683(-FT) showed strong preferential recognition by NAbs IgG1b12 and 2G12 relative to the gp120 monomer, in contrast to poorly neutralizing MAbs F105, F91, 17b, 48d, and 39F which showed reduced levels of binding, and C11, A32, and 30D which did not bind the stabilized oligomer [Yang2002].
- 17b: CD4 residue Phe43 significantly contributes to the affinity of CD4-gp120 interactions – despite decreased affinities for gp120, CD4 proteins and CD4-mimetic peptides lacking a Phe side-chain enhance binding of gp120 to 17b in a manner similar to Phe-bearing ligands indicating the Phe42 interaction is not critical for CD4-induced conformational changes in gp120 [Dowd2002]
- 17b: A series of mutational changes were introduced into the YU2 gp120 that favored different conformations – 375 S/W seems to favor a conformation of gp120 closer to the CD4-bound state, and is readily bound by sCD4 and CD4i MAbs (17b, 48d, 49e, 21c and 23e) but binding of anti-CD4BS MAbs (F105, 15e, IgG1b12, 21h and F91 was markedly reduced – IgG1b12 failed to neutralize this mutant, while neutralization by 2G12 was enhanced – 2F5 did not neutralize either WT or mutant, probably due to polymorphism in the YU2 epitope – another mutant, 423 I/P, disrupted the gp120 bridging sheet, favored a different conformation and did not bind CD4, CCR5, or CD4i antibodies, but did bind to CD4BS MAbs [Xiang2002b]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 17b: Five CD4i MAbs were studied, 17b, 48d and three new MAbs derived by Epstein-Barr virus transformation of PBMC from an HIV+ long term non-progressor – 23e and 21c were converted to hybridomas to increase Ab production – all compete with the well-characterized 17b CD4i MAb in an ELISA antigen capture assay – critical binding residues are mapped and the CD4i MAb epitopes were distinct but share a common element near isoleucine 420, also important for CCR5 binding, and all five can block CCR5 binding to a sCD4-gp120 complex – the MAb 48d has the epitope most similar to the CCR5 binding site [Xiang2002a]
- 17b: Truncation of the gp41 cytoplasmic domain of X4, R5, and X4R5 viruses forces a conformation that more closely resembles the CD4 bound state of the external Envelope, enhancing binding of CD4i MAbs 17b and 48d and of CD4BS MAbs F105, b12, and in most cases of glycosylation site dependent MAb 2G12 and the anti-gp41 MAb 246D – in contrast, binding of the anti-V2 MAb 697D and the anti-V3 MAb 694/98D were not affected – viruses bearing the truncation were more sensitive to neutralization by MAbs 48d, b12, and 2G12 – the anti-C5 MAb 1331A was used to track levels of cell surface expression of the mutated proteins [Edwards2002]
- 17b: HIV-1 gp160ΔCT (cytoplasmic tail-deleted) proteoliposomes (PLs) containing native, trimeric envelope glycoproteins from R5 strains YU2 and JRFL, and X4 strain HXBc2, were made in a physiologic membrane setting as candidate immunogens for HIV vaccines—2F5 bound to gp160ΔCT with a reconstituted membrane ten-fold better than the same protein on beads—anti-CD4BS MAbs IgG1b12 and F105, A32 (C1-C4), C11 (C1-C5), and 39F (V3) MAbs bound gp160ΔCT PLs indistinguishably from gp160ΔCT expressed on the cell surface—non-neutralizing MAbs C11 and A32 bound with lower affinity than NAb IgG1b12—the MAb 17b was sCD4 inducible on gp160ΔCT PL [Grundner2002].
- 17b: gp120 mutants were used to define the CXCR4 binding site using CXCR4 displayed on paramagnetic proteoliposomes (PMPLs) to reduce non-specific gp120 binding—basic residues in the V3 loop and the β19 strand (RIKQ, positions 419-422) were involved, and deletion of the V1-V2 loops allowed CD4-independent CXCR4 binding—MAbs 17b (CD4i) and F105 (CD4BS) were used to study conformational changes in the mutants—the affinity of ΔV1 and ΔV1-V2 for 17b was dramatically increased and no longer inducible in the presence of sCD4—V3 mutants R298A and R327A were not recognized by 17b except in the presence of sCD4—mutations in the β19 strand dramatically reduced 17b affinity in the presence or absence of sCD4, consistent with known 17b contact residues in this region [Basmaciogullari2002].
- 17b: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain [Zhang2002]
- 17b: The two N-terminal domains of CD4, termed D1 and D2, when expressed in the absence of the remaining domains of CD4 retain the capacity to bind to gp120—coding sequences of D1D2 and Igαtp were fused to create a large, multivalent rec protein D1D2Igαtp, which, unlike CD4, does not enhance infection at sub-optimal concentrations—the MAb 17b can also enhance viral replication at sub-optimal concentrations, but D1D2-Igα inhibited the 17b enhancement of two primary isolates [Arthos2002].
- 17b: NIH AIDS Research and Reference Reagent Program: 4091

969	21c	Env	gp120 (IIIB, J62)		L	HIV-1 infection	human (IgG)

Ab type CD4i **Donor** James Robinson, Tulane University, New Orleans, LA, USA
References Xiang2002a, Xiang2002b

- 21c: Five CD4i MAbs were studied, 17b, 48d and three new MAbs derived by Epstein-Barr virus transformation of PBMC from an HIV+ long term non-progressor – 23e and 21c were converted to hybridomas to increase Ab production – all compete with the well-characterized 17b CD4i MAb in an ELISA antigen capture assay – critical binding residues are mapped and the CD4i MAb epitopes were distinct but share a common element near isoleucine 420, also important for CCR5 binding, and all five can block CCR5 binding to a sCD4-gp120 complex – the MAb 48d has the epitope most similar to the CCR5 binding site [Xiang2002a]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 21c: A series of mutational changes were introduced into the YU2 gp120 that favored different conformations – 375 S/W seems to favor a conformation of gp120 closer to the CD4-bound state, and is readily bound by sCD4 and CD4i MAbs (17b, 48d, 49e, 21c and 23e) but binding of anti-CD4BS MAbs (F105, 15e, IgG1b12, 21h and F91 was markedly reduced – IgG1b12 failed to neutralize this mutant, while neutralization by 2G12 was enhanced – 2F5 did not neutralize either WT or mutant, probably due to polymorphism in the YU2 epitope – another mutant, 423 I/P, disrupted the gp120 bridging sheet, favored a different conformation and did not bind CD4, CCR5, or CD4i antibodies, but did bind to CD4BS MAbs [Xiang2002b]

970 23e Env gp120 (IIIB, J62) L HIV-1 infection human (IgG)

Ab type CD4i **Donor** James Robinson, Tulane University, New Orleans, LA, USA

References Xiang2002a, Xiang2002b

- 23e: Five CD4i MAbs were studied, 17b, 48d and three new MAbs derived by Epstein-Barr virus transformation of PBMC from an HIV+ long term non-progressor – 23e and 21c were converted to hybridomas to increase Ab production – all compete with the well-characterized 17b CD4i MAb in an ELISA antigen capture assay – critical binding residues are mapped and the CD4i MAb epitopes were distinct but share a common element near isoleucine 420, also important for CCR5 binding, and all five can block CCR5 binding to a sCD4-gp120 complex – the MAb 48d has the epitope most similar to the CCR5 binding site [Xiang2002a]
- 23e: A series of mutational changes were introduced into the YU2 gp120 that favored different conformations – 375 S/W seems to favor a conformation of gp120 closer to the CD4-bound state, and is readily bound by sCD4 and CD4i MAbs (17b, 48d, 49e, 21c and 23e) but binding of anti-CD4BS MAbs (F105, 15e, IgG1b12, 21h and F91 was markedly reduced – IgG1b12 failed to neutralize this mutant, while neutralization by 2G12 was enhanced – 2F5 did not neutralize either WT or mutant, probably due to polymorphism in the YU2 epitope – another mutant, 423 I/P, disrupted the gp120 bridging sheet, favored a different conformation and did not bind CD4, CCR5, or CD4i antibodies, but did bind to CD4BS MAbs [Xiang2002b]

971 48d (4.8d, 4.8D) Env gp120 L P (weak) HIV-1 infection human (IgG1κ)

Ab type CD4i **Donor** James Robinson, Tulane University, New Orleans, LA, USA

References Thali1993, Moore1993a, Moore1993d, Thali1994, Moore1994b, D'Souza1995, Sattentau1995a, Wyatt1995, Sattentau1995b, Moore1996, Poignard1996a, Trkola1996a, Binley1997a, Li1997, Weinberg1997, Lee1997, Ugolini1997, Wyatt1997, Parren1997c, Frankel1998, Wyatt1998a, Mondor1998, Parren1998a, Sullivan1998b, Yang1998, Binley1998, Stamatatos1998, Oscherwitz1999a, Hoffman1999, Fortin2000, Ly2000, Park2000, Yang2000, Salzwedel2000, Kolchinsky2001, Verrier2001, Golding2002b, Yang2002, Xiang2002b, Xiang2002a, Edwards2002, Zhang2002

- 48d: 48d and 17b have similar epitopes, and the pair are unique among human and rodent MAbs
- 48d: Epitope is better exposed upon CD4 binding to gp120 – competes with ICR 39.13, 15e and 21h, anti-CD4 binding site MAbs – inhibited by anti-CD4BS MAb ICR 39.13g and linear anti-C4 MAbs G3-42 and G3-508 – 113 D/R, 252 R/W, 257 T/A or G, 370 E/D, 382 F/L, 420 I/R, 421 K/L, 433A/L, 438 P/R and 475 M/S confer decreased sensitivity to neutralization [Thali1993]
- 48d: Called 4.8d – Neutralizes IIIB – reactive with SF-2 gp120 – does not inhibit HIV-1 sera from binding to IIIB gp120 [Moore1993a]
- 48d: Binding of 48d is much more influenced by sequence variation among molecular clones of LAI than is binding of 17b [Moore1993d]
- 48d: A mutation in gp41, 582 A/T, confers resistance to neutralization (also confers resistance to MAbs F105, 21h, 15e and 17b) [Thali1994]
- 48d: Poor cross-reactivity with gp120 from most clades [Moore1994b]
- 48d: Called 4.8D – Found to neutralize MN, but not JRCSF, two B subtype primary isolates, or a D subtype primary isolate, by most labs in a multi-laboratory study involving 11 labs[D'Souza1995]
- 48d: Studies using a V1/V2 deletion mutant demonstrated that enhanced binding of 48d in the presence of sCD4 involves the V1/V2 loops, with more significant involvement of V2 – similar effect observed for 17b and A32 [Wyatt1995]
- 48d: Formalin inactivation of virus at 0.1% formalin for 10 hours at 4 degrees was optimal for inactivation of virus while maintaining epitope integrity [Sattentau1995c]
- 48d: Binds with similar affinity to monomer and oligomer, moderate association rate, potent neutralization – this is in contrast to 17b, which has very different kinetics [Sattentau1995b]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 48d: Many MAbs inhibit binding (anti-C1, -C5, -C4, -CD4BS) – anti-C1-C4 discontinuous epitope MAbs A32 and 2/11c enhance binding – reciprocal enhanced binding with some anti-V2 MAbs [Moore1996]
- 48d: Binding resulted in gp120 dissociation from virion, mimicking sCD4, and exposure of the gp41 epitope of MAb 50-69, in contrast to CD4BS MAbs [Poignard1996a]
- 48d: Neutralizes JR-FL – slightly inhibits gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study [Trkola1996a]
- 48d: One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB env – all Ab combinations tested showed synergistic neutralization – 48d has synergistic response with MAbs 694/98-D (anti-V3) and F105 [Li1997]
- 48d: 48d binds to the IIIB protein and not IIIB V3 peptide, while binding to the Can0A V3 peptide, suggesting Can0A V3 is a conformer that mimics the 48d, (but not 17b), epitope [Weinberg1997]
- 48d: Prefers CD4-gp120 complex to gp120 alone, but does not enhance fusion, in contrast to MAb CG10, in fact it inhibits syncytium formation [Lee1997]
- 48d: Viral binding inhibition by 48d was strongly correlated with neutralization (all other neutralizing MAbs tested showed some correlation except 2F5) [Ugolini1997]
- 48d: Binds efficiently to sgp120 but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding [Wyatt1997]
- 48d: Neutralizes TCLA strains, but not primary isolates [Parren1997c]
- 48d: Summary of the implications of the crystal structure of the core of gp120 bound to CD4 and 17b with what is known about mutations that reduce NAb binding – probable mechanism of neutralization of 48d is interference with chemokine receptor binding – CD4 binding increases exposure of epitope due to V2 loop movement – 88N, 117K, 121K, 256S, 257T, N262, delta V3, E370, E381, F 382, R 419, I 420, K 421, Q 422, I 423, W 427, Y 435, P 438, M 475 mutations in HXBc2 (IIIB) decrease binding [Wyatt1998a]
- 48d: Inhibits binding of Hx10 to both CD4 positive and CD4 negative HeLa cells [Mondor1998]
- 48d: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren1998a]
- 48d: CD4i MAbs 17b and 48d compete with MAb CG10, and the binding sites may overlap – MAb A32 enhances binding of 17b, 48d and CG10 [Sullivan1998b]
- 48d: A neutralization assay was developed based on hemi-nested PCR amplification of the LTR (HNPCR) – LTR-HNPCR consistently revealed HIV DNA and was shown to be a rapid, specific and reliable neutralization assay based on tests with 6 MAbs and 5 isolates [Yang1998]
- 48d: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer – CD4i MAbs 17b and 48d bound better to the deleted protein than to wild type [Binley1998]
- 48d: Deleting the V2 loop of neutralization-resistant HIV-1 isolate SF162 does not abrogate its replication in PBMC or macrophages, but it enhances its neutralization sensitivity to sera from patients with B clade infection up to 170-fold, and also enhances sensitivity to sera from clades A through F – deletion of V2 but not V1 enabled neutralization by CD4i MAbs 17b and 48d [Stamatatos1998]
- 48d: Infection of dendritic cells cultured from CD14+ blood cells or from cadaveric human skin was blocked by neutralizing MAbs IgG1b12, or 2F5 and 2G12 delivered together, but not by control non-neutralizing anti-gp120 MAb 4.8D, indicating that NAbs could interrupt early mucosal transmission events [Frankel1998]
- 48d: A CD4-independent viral variant of IIIB, IIIBx, was generated on CXCR4-expressing cells – IIIBx exhibited greater exposure of the 17b and 48d epitopes and enhanced neutralization by CD4i MAbs and by polyclonal human sera [Hoffman1999]
- 48d: Called 4.8D – host encoded intercellular adhesion molecule (ICAM-1) is incorporated by the HIV-1 virion and enhances viral infectivity – ICAM-1 does not modify virus sensitivity to antibodies 0.5beta or 4.8D or sCD4, but neutralizing ability of F105 was diminished in ICAM bearing virions in the presence of lymphocyte function-association antigen-1 (LFA-1) Ab [Fortin2000]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 48d: SF162 is a neutralization-resistant HIV-1 isolate – N-linked glycosylation modifications in the V2 loop of the SF162 gp120 revealed that these sites prevent neutralization by CD4BS MAbs (IgG1b12 and IgGCD4), and protect against neutralization by V3 MAbs (447-D and 391-95D) – V2-region glycosylation site mutations did not alter neutralization resistance to V2 MAbs (G3.4 and G3.136) or CD4i MAbs (17b and 48d) – V2 glycosylation site modification allows infection of macrophages, probably due to glycosylated forms requiring fewer CCR5 molecules for viral entry [Ly2000]
- 48d: Six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20-100 fold more efficient at neutralizing the sensitive form – the mutation L544P reduced binding of all MAbs against gp120 by causing conformational changes [Park2000]
- 48d: sCD4 can activate fusion between effector cells expressing Env and target cells expressing coreceptor (CCR5 or CXCR4) alone without CD4 – CD4i MAbs 17b and 48d have little effect on a standard cell fusion assay but potently block sCD4 activated fusion [Salzwedel2000]
- 48d: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) that preserve and expose some neutralizing epitopes while occluding some non-neutralizing epitopes – CD4BS MAbs (F105 and F91) and CD4i (17b and 48d) recognized gp140-GNC4 as well as gp120 or gp140 – non-neutralizing MAbs C11, A32, 522-149, M90, and #45 bound to the gp140-GNC4 glycoprotein at reduced levels compared to gp120 – MAbs directed at the extreme termini of gp120 C1 (135/9 and 133/290) and C5 (CRA-1 and M91) bound efficiently to gp140-GNC4 [Yang2000]
- 48d: Mutations in two glcosylation sites in the V2 region of HIV-1 ADA at positions 190 and 197 (187 DNTSYRLINCNTS 199) cause the virus to become CD4-independent and able to enter cells through CCR5 alone – these same mutations tended to increase the neutralization sensitivity of the virus, including to 48d – only the CD4i antibodies 17b and 48d showed an increased affinity of the CD4 independent viruses relative to wild-type [Kolchinsky2001]
- 48d: Called 4.8d – A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6 – six gave significant neutralization at 2 to 10 ug/ml: 2F5, 50-69, IgG1b12, 447-52D, 2G12, and 670-D six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98-6, and 1281 – no synergy, only additive effects were seen for pairwise combinations of MAbs, and antagonism was noted between gp41 MAbs 50-69 and 98-6, as well as 98-6 and 2F5 [Verrier2001]
- 48d: The fusion process was slowed by using a suboptimal temperature (31.5 C) to re-evaluate the potential of Abs targeting fusion intermediates to block HIV entry – preincubation of E/T cells at 31.5 C enabled polyclonal anti-N-HR Ab and anti-six-helix bundle Abs to inhibit fusion, indicating six-helix bundles form prior to fusion – the preincubation 31.5 C step did not alter the inhibitory activity of neutralizing Abs anti-gp41 2F5, or anti-gp120 2G12, IG1b12, 48d, and 17b [Golding2002b]
- 48d: Uncleaved soluble gp140 (YU2 strain, R5 primary isolate) can be stabilized in an oligomer by fusion with a C-term trimeric GCN4 motif or using a T4 trimeric motif derived from T4 bacteriophage fibritin – stabilized oligomer gp140 delta683(-FT) showed strong preferential recognition by NAbs IgG1b12 and 2G12 relative to the gp120 monomer, in contrast to poorly neutralizing MAbs F105, F91, 17b, 48d, and 39F which showed reduced levels of binding, and C11, A32, and 30D which did not bind the stabilized oligomer [Yang2002]
- 48d: A series of mutational changes were introduced into the YU2 gp120 that favored different conformations – 375 S/W seems to favor a conformation of gp120 closer to the CD4-bound state, and is readily bound by sCD4 and CD4i MAbs (17b, 48d, 49e, 21c and 23e) but binding of anti-CD4BS MAbs (F105, 15e, IgG1b12, 21h and F91 was markedly reduced – IgG1b12 failed to neutralize this mutant, while neutralization by 2G12 was enhanced – 2F5 did not neutralize either WT or mutant, probably due to polymorphism in the YU2 epitope – another mutant, 423 I/P, disrupted the gp120 bridging sheet, favored a different conformation and did not bind CD4, CCR5, or CD4i antibodies, but did bind to CD4BS MAbs [Xiang2002b]
- 48d: Five CD4i MAbs were studied, 17b, 48d and three new MAbs derived by Epstein-Barr virus transformation of PBMC from an HIV+ long term non-progressor – 23e and 21c were converted to hybridomas to increase Ab production – all compete with the well-characterized 17b CD4i MAb in an ELISA antigen capture assay – critical binding residues are mapped and the CD4i MAb epitopes were distinct but share a common element near isoleucine 420, also important for CCR5 binding, and all five can block CCR5 binding to a sCD4-gp120 complex – the MAb 48d has the epitope most similar to the CCR5 binding site [Xiang2002a]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 48d: Truncation of the gp41 cytoplasmic domain of X4, R5, and X4R5 viruses forces a conformation that more closely resembles the CD4 bound state of the external Envelope, enhancing binding of CD4i MAbs 17b and 48d and of CD4BS MAbs F105, b12, and in most cases of glycosylation site dependent MAb 2G12 and the anti-gp41 MAb 246D – in contrast, binding of the anti-V2 MAb 697D and the anti-V3 MAb 694/98D were not affected – viruses bearing the truncation were more sensitive to neutralization by MAbs 48d, b12, and 2G12 – the anti-C5 MAb 1331A was used to track levels of cell surface expression of the mutated proteins [Edwards2002]
- 48d: Called 4.8D – A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain [Zhang2002]
- 48d: NIH AIDS Research and Reference Reagent Program: 1756

972	49e	Env	gp120 (IIIB, J62)		L	HIV-1 infection	human (IgG)

Ab type CD4i **Donor** James Robinson, Tulane University, New Orleans, LA, USA
References Xiang2002a, Xiang2002b

- 49e: Five CD4i MAbs were studied, 17b, 48d and three new MAbs derived by Epstein-Barr virus transformation of PBMC from an HIV+ long term non-progressor – 23e and 21c were converted to hybridomas to increase Ab production – all compete with the well-characterized 17b CD4i MAb in an ELISA antigen capture assay – critical binding residues are mapped and the CD4i MAb epitopes were distinct but share a common element near isoleucine 420, also important for CCR5 binding, and all five can block CCR5 binding to a sCD4-gp120 complex – the MAb 48d has the epitope most similar to the CCR5 binding site [Xiang2002a]
- 49e: A series of mutational changes were introduced into the YU2 gp120 that favored different conformations – 375 S/W seems to favor a conformation of gp120 closer to the CD4-bound state, and is readily bound by sCD4 and CD4i MAbs (17b, 48d, 49e, 21c and 23e) but binding of anti-CD4BS MAbs (F105, 15e, IgG1b12, 21h and F91 was markedly reduced – IgG1b12 failed to neutralize this mutant, while neutralization by 2G12 was enhanced – 2F5 did not neutralize either WT or mutant, probably due to polymorphism in the YU2 epitope – another mutant, 423 I/P, disrupted the gp120 bridging sheet, favored a different conformation and did not bind CD4, CCR5, or CD4i antibodies, but did bind to CD4BS MAbs [Xiang2002b]

973	X5	Env	(JRFL)		P	HIV-1 infection	human

Ab type CD4i
References Moulard2002

- X5: The human Fab X5 was selected from a phage display library derived from an HIV-1 positive donor with a highly neutralizing serum – it was selected for binding to purified gp120-CD4-coreceptor complexes – the Fab neutralizes PBMC infection by a selection of HIV-1 primary isolates from clades A, B, C, D, E, F, and G, and neutralizes R5, X4, and R5X4 isolates – it binds to a conserved epitope on gp120 induced by CD4 binding, its binding is slightly enhanced by CCR5 binding – while CD4i MAb 17b binds the CCR5 binding site, X5 also competes with Fab b12 which overlaps with the CD4 binding site, suggesting the epitope for is near both the CD4 and CCR5 binding sites [Moulard2002]

974	T22	Env	gp120 (IIIB)			Vaccine	murine (IgG)

Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140
Ab type Env oligomer **Donor** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References Earl1994, Otteken1996, Sugiura1999

- T22: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response [Earl1994]
- T22: Pulse label experiments of 4 MAbs (D20, D27, T20, and T22) binding to noncleavable gp140 revealed that these anti-CD4BS MAbs bound with a delay, and that the epitope formed with a t 1/2 of about 10 minutes [Otteken1996]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• T22: A comparison of 25 gp120 specific, conformation dependent MAbs was done – T22 is part of a group of MAbs labeled AII – all AII MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, and could only partially blocked CD4 binding [Sugiura1999]					
975	polyclonal	Env	gp41			Vaccine	rabbit (IgG)
		Vaccine *Vector/Type:* peptide *Adjuvant:* gp41 N-HR and C-HR helical peptides **Ab type** N-HR, C-HR, and six-helix bundle **References** deRosny2001, Golding2002b • A panel of Abs against gp41 heptad repeats N-HR, C-HR, and self-assembled stable N-HR and C-HR six helix bundles were generated [deRosny2001] • The fusion process was slowed by using a suboptimal temperature (31.5 C) to re-evaluate the potential of Abs targeting fusion intermediates to block HIV entry – preincubation of E/T cells at 31.5 C enabled polyclonal anti-N-HR Ab and anti-six-helix bundle Abs to inhibit fusion, indicating six-helix bundles form prior to fusion – the preincubation 31.5 C step did not alter anti-C-HR Abs inability to inhibit fusion [Golding2002b]				
976	2A2	Env	gp41		no	HIV-1 infection	human (IgG1κ)
		Ab type N-term **References** Weissenhorn1996 • Soluble gp41(21-166) forms a rod like structure that can be visualized with electron microscopy, and 2A2 binds to one end of the rod [Weissenhorn1996]					
977	AC4	Env	gp120 (IIIB)		yes	Vaccine	murine
		Vaccine *Vector/Type:* recombinant protein *HIV component:* gp160 **Ab type** N-term **References** Dickey2000 • AC4: Three MABs, ID6, AC4, and AD3 that bind to a discontinuous N-term first 204 aa of gp120 and generate ADCC were elicited through vaccination of BALBc mice with rec gp160 – these MAbs do not depend on glycosylation and are cross-reactive with viruses from clades B and CRF01(AE) [Dickey2000]					
978	AD3	Env	gp120 (IIIB)		yes	Vaccine	murine
		Vaccine *Vector/Type:* recombinant protein *HIV component:* gp160 **Ab type** N-term **References** Dickey2000, Cook1994 • AD3: There may be two Abs with this name that bind to the N-term region of gp120 [Cook1994, Dickey2000] • AD3: Three MABs, ID6, AC4, and AD3 that bind to a discontinuous N-term first 204 aa of gp120 and generate ADCC were elicited through vaccination of BALBc mice with rec gp160 – these MAbs do not depend on glycosylation and are cross-reactive with viruses from clades B and CRF01(AE) [Dickey2000]					
979	AD3	Env	gp120 (BH10)				murine (IgG1)
		Ab type N-term **References** Ugen1993, Cook1994, Dickey2000 • AD3: There may be two Abs with this name that bind to the N-term region of gp120 [Cook1994, Dickey2000] • AD3: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – MAbs against the N-terminal half of gp120 do not inhibit gp120 binding to GalCer – binding of GalCer to gp120 does not inhibit MAb binding [Cook1994] • AD3: NIH AIDS Research and Reference Reagent Program: 2342					
980	ID6	Env	gp120 (1–193 BH10)				murine (IgG1)
		Ab type N-term **References** Ugen1993, Cook1994, Dickey2000 • ID6: There may be two Abs with this name that bind to the N-term region of gp120 [Cook1994, Dickey2000]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• ID6: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – MAbs against the N-terminal half of gp120 do not inhibit gp120 binding to GalCer – binding of GalCer to gp120 does not inhibit MAb binding [Cook1994] • ID6: NIH AIDS Research and Reference Reagent Program: 2343					
981	ID6	Env	gp120 (IIIB)		yes	Vaccine	murine (IgG2a)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* gp160 **Ab type** N-term **References** Dickey2000, Cook1994 • ID6: There may be two Abs with this name that bind to the N-term region of gp120 [Cook1994, Dickey2000] • ID6: Three MABs, ID6, AC4, and AD3 that bind to a discontinuous N-term first 204 aa of gp120 and generate ADCC were elicited through vaccination of BALBc mice with rec gp160 – these MAbs do not depend on glycosylation and are cross-reactive with viruses from clades B and CRF01(AE) [Dickey2000]					
982	11/68b	Env	gp120		L (HXB2)	Vaccine	rat (IgG1)
		Vaccine *Vector/Type:* recombinant protein *Strain:* BH10 *HIV component:* gp120 **Ab type** V1-V2 **Donor** Shotton and Dean **References** McKeating1993b, Shotton1995, Peet1998 • 11/68b: Changes at residues 183/184 (PI/SG) within V2, 435 (Y/H) in C4, abrogate binding [McKeating1993b] • 11/68b: 435 (Y/H) in C4 does not abrogate binding (John Moore, per comm, 1996) • 11/68b: Cross-competes with MAbs 62c, 66c, 66a, and CRA-4 – similar to MAb 62c – HXB2 neutralization escape mutant had a D/N substitution at residue 185 – non-reciprocal inhibition of binding of CRA-3 and CRA-6 [Shotton1995] • 11/68b: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind – 11/68b was not affected by V3 serine substitutions – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions [Peet1998] • 11/68b: UK Medical Research Council AIDS reagent: ARP3041					
983	62c	Env	gp120		no	Vaccine	rat (IgG1)
		Vaccine *Vector/Type:* recombinant protein *Strain:* BH10 *HIV component:* gp120 **Ab type** V1-V2 **References** Shotton1995 • 62c: Cross-competes with MAbs 11/68b, 66c, 66a, and CRA-4 – same cross-competition group as MAb 11/68b – non-reciprocal inhibition of binding of CRA-3 and CRA-6 – substitutions 176-177 FY/AT, 179-180 LD/DL, 183-184 PI/SG, and 191-193 YSL/GSS abrogate binding – binds but does not neutralize Hx10 [Shotton1995] • 62c: UK Medical Research Council AIDS reagent: ARP3075					
984	CRA-6 (CRA6)	Env	gp120		no		murine
		Ab type V1-V2 **References** Shotton1995 • CRA-6: Called CRA6 – same competition group as CRA-3 [Shotton1995]					
985	L15	Env	gp120		P (weak)	HIV-1 infection	human (IgG1)
		Ab type V1-V2 **References** Ditzel1997, Parren1997c					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• L15: gp120 immobilized on solid phase by capture with anti-CD4 BS MAb L72 was used for selection of Fabs – 2 anti-V2 Fabs were obtained with very similar epitopes, L15 and L17 – deletions in V1 and V2 abolished binding, and rodent anti-V2 MAbs SC258, CRA3, G3-G4,G3-136, BAT-085, and 52-684 all compete with L15 [Ditzel1997] • L15: Does not neutralize TCLA strains but neutralizes some primary isolates weakly [Parren1997c]					
986	T52	Env	gp120 (IIIB)			Vaccine	murine (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140 **Ab type** V1-V2 **Donor** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD **References** Earl1994, Sugiura1999 • T52: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response [Earl1994] • T52: A comparison of 25 gp120 specific, conformation dependent MAbs was done – T52 is one of two MAbs labeled B-II, that had limited cross-reactivity with seven clade B isolates and did not fully blocked CD4 binding – deletion of V1/V2 loops abrogated binding [Sugiura1999]					
987	T54	Env	gp120 (IIIB)		no	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140 **Ab type** V1-V2 **Donor** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD **References** Earl1994, Sugiura1999 • T54: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response [Earl1994] • T54: A comparison of 25 gp120 specific, conformation dependent MAbs was done – T54 is one of two MAbs labeled B-II, that had limited cross-reactivity with seven clade B isolates and did not fully blocked CD4 binding – deletion of V1/V2 loops abrogated binding [Sugiura1999]					
988	polyclonal	Env	Env		yes	HIV-1 infection	human
		Ab type V1-V2 and V3-V5 **References** Gordon2000 • Primary isolates have great differences in susceptibility to neutralization – the variation in V1V2 and V3-V5 was measured by HTA in a set of viruses with a range of neutralization susceptibilities, and greater variability was uncorrelated with resistance to neutralization [Gordon2000]					
989	1088	Env	gp120				
		Ab type V2 **References** Berman1997 • 1088: Binds weakly to 2/7 isolates from breakthrough cases from a MN gp120 vaccine trial [Berman1997]					
990	110-B	Env	gp120		no	Vaccine	murine
		Vaccine *Vector/Type:* infected-cell lysate *Strain:* BRU *HIV component:* virus **Ab type** V2 **Donor** Hybridolabs, Institute Pasteur, Paris, France **References** Moore1993b • 110-B: specific for BH10, does not bind to MN, RF, or SF-2 gp120 – binding inhibited by deletion of the V2 loop, and the following amino acid substitutions: 168 K/L, 176/177 FY/AT, 179/180 LD/DL, 183/184 PI/SG, and 192-194 YSL/GSS [Moore1993b]					
991	1357	Env	gp120				human (IgG1κ)
		Ab type V2 **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center) **References** Nyambi1998, Gorny2000a, Nyambi2000 • 1357: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 5 anti-V2 MAbs, which showed weak and sporadic binding, with the most frequent binding to C and D clades [Nyambi2000]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 1357: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – V2 Abs 697-D, 1361, and 1357 tended to bind very weakly with a similar pattern of specificity to virions, but bound well to soluble gp120: weak binding only to subtype D MAL [Nyambi1998] • 1357: Blocks binding of MAb 697-D to rgp120, and doesn't react with a protein from which V1V2 has been deleted – binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – V2 MAbs 697-D, 1357 and 1361 favored the monomer by approximately 2 fold [Gorny2000a] • 1357: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 5 anti-V2 MAbs, which showed weak and sporadic binding, with the most frequent binding to C and D clades [Nyambi2000]				
992	1361	Env	gp120			Vaccine	human (IgG1κ)
		Vaccine *Vector/Type:* protein *HIV component:* gp120 **Ab type** V2 **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center) **References** Nyambi1998, Gorny2000a, Nyambi2000 • 1361: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – V2 Abs 697-D, 1361, and 1357 tended to bind weakly with a similar pattern of specificity to virions, but bound well to soluble gp120: weak binding to 1/4 B clade viruses (CA5), and also weak binding to a subtype D virus, MAL [Nyambi1998] • 1361: Blocks binding of MAb 697-D to rgp120, and doesn't react with a protein from which V1V2 has been deleted – binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – V2 MAbs 697-D, 1357 and 1361 favored the monomer by approximately 2 fold [Gorny2000a] • 1361: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 5 anti-V2 MAbs, which showed weak and sporadic binding, with the most frequent binding to C and D clades [Nyambi2000]				
993	1393A	Env	gp120			HIV-1 infection	
		Ab type V2 **References** Nyambi2000 • 1393A: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 5 anti-V2 MAbs, which showed weak and sporadic binding, with the most frequent binding to C and D clades [Nyambi2000]					
994	66a	Env	gp120		L (HXB2)	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *Strain:* BH10 *HIV component:* gp120 **Ab type** V2 **References** Shotton1995 • 66a: Substitutions 176-177 FY/AT, 179-180 LD/DL, 183-184 PI/SG, and 191-193 YSL/GSS abrogate binding – same competition group as CRA4 [Shotton1995] • 66a: UK Medical Research Council AIDS reagent: ARP3074					
995	66c	Env	gp120		L (HXB2)	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *Strain:* BH10 *HIV component:* gp120 **Ab type** V2 **References** Shotton1995					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 66c: Substitutions 176-177 FY/AT, 179-180 LD/DL, 183-184 PI/SG, and 191-193 YSL/GSS abrogate binding – same competition group as CRA4 [Shotton1995]					
996	684-238 (52-684-238, 52-684)	Env	gp120		L	Vaccine	murine
		Vaccine *Vector/Type:* purified protein *Strain:* IIIB *HIV component:* gp120 **Ab type** V2 **Donor** Gerry Robey, Abbott Laboratories **References** Moore1993b, Thali1993, Gorny1994, Ditzel1995, Moore1996, Ditzel1997 • 684-238: Specific for BH10 or HXB2, does not bind to MN, RF, or SF-2 gp120 – neutralizes BH10 – binding inhibited by deletion of the V2 loop, and the following amino acid substitutions: 176/177FY/AT, 179/180LD/DL, 183/184PI/SG, and 192-194YSL/GSS [Moore1993b] • 684-238: Weakly neutralizing, IC 50 = 84 mug/ml [Gorny1994] • 684-238: Does not compete with IgG1b12, reciprocal inhibition with MAbs L39, L40, and L78 [Ditzel1995] • 684-238: Limited reciprocal enhancement of binding with anti-V3 and C4 region antibodies – reciprocal inhibition with V2 region antibodies [Moore1996]					
997	830A	Env	gp120			HIV-1 infection	
		Ab type V2 **References** Nyambi2000 • 830A: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 5 anti-V2 MAbs, which showed weak and sporadic binding, with the most frequent binding to C and D clades [Nyambi2000]					
998	CRA-3 (CRA3)	Env	gp120		no	Vaccine	murine (IgG2a)
		Vaccine *Vector/Type:* recombinant protein *Strain:* BH10 *HIV component:* gp120 **Ab type** V2 **Donor** Mark Page, NIBSC AIDS reagent project, Potters Bar, Herts, UK **References** Moore1993a, Moore1993b, Thali1993, Shotton1995, Moore1996, Ditzel1997 • CRA-3: Conformational, does not bind well to denatured gp120 [Moore1993a] • CRA-3: specific for BH10 or HXB2, does not bind to MN, RF, or SF-2 gp120 – binding inhibited by deletion of the V2 loop, and the following amino acid substitutions: 176/177 FY/AT, 179/180 LD/DL, 183/184 PI/SG, and 192-194 YSL/GSS – epitope probably involves stem of V1/V2 loop structure [Moore1993b] • CRA-3: Many MAbs enhance binding, including some anti-C5, C1, V4, and C4 MAbs – enhances binding of only a small number of anti-V3 loop MAbs [Moore1996] • CRA-3: Called CRA3 – Same competition group as CRA6 [Shotton1995] • CRA-3: UK Medical Research Council AIDS reagent: ARP324					
999	CRA-4 (CRA4)	Env	gp120		L (HXB2)	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *Strain:* BH10 *HIV component:* gp120 **Ab type** V2 **Donor** Mark Page, NIBS, MRC AIDS reagent repository, ARP 325 **References** McKeating1993b, Moore1993a, Moore1993b, Thali1993, Shotton1995, Moore1996 • CRA-4: Changes at residues 191/192/193 (YSL/GSS) within V2, 435 (Y/H) in C4, abrogate binding – type-specific neutralization [McKeating1993b] • CRA-4: Conformational, does not bind well to denatured gp120 [Moore1993a] • CRA-4: Specific for BH10 and HXB2, does not bind to MN, RF, or SF-2 gp120 – binding inhibited by deletion of the V2 loop, and the following amino acid substitutions: 176/177 FY/AT, 179/180 LD/DL, 183/184 PI/SG, and 192-194 YSL/GSS [Moore1993b] • CRA-4: Cross-competes with MAbs 11/68b, 62c, 66c, 66a – similar to 66c and 66a – non-reciprocal inhibition by MAbs 12b, 60b and CRA-6 [Shotton1995] • CRA-4: The only MAbs that enhanced binding were anti-V3 MAb 5G11 and anti-C1 MAb 135/9 binding – reciprocal inhibition of anti-V2 MAbs [Moore1996]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• CRA-4: UK Medical Research Council AIDS reagent: ARP325					
1000	L17	Env	gp120				human Fab
		Ab type V2					
		References Ditzel1997, Parren1998a					
		• L17: The rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142-10 > DA48 > L17) was markedly different than Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142-10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren1998a]					
1001	SC258 (52-581-SC258)	Env	gp120		L	Vaccine	murine
		Vaccine *Vector/Type:* purified protein *Strain:* IIIB *HIV component:* gp120					
		Ab type V2 **Donor** Gerry Robey, Abbott Laboratories					
		References Moore1993b, Thali1993, Gorny1994, Yoshiyama1994, Moore1994b, Ditzel1995, Moore1996, Trkola1996a, Ditzel1997, He2002					
		• SC258: Called 52-581-SC258 – binds to BH10, MN, and RF gp120 – neutralizes BH10 – binding inhibited by deletion of the V2 loop, and the following amino acid substitutions: 176/177 FY/AT, 179/180 LD/DL, 183/184 PI/SG, and 192-194 YSL/GSS [Moore1993b]					
		• SC258: HIV-1 RF V2 substitutions 177 Y/H and 179 L/P in the V2 loop of RF reduce affinity – 177 Y/H inhibits SC258 neutralization [Yoshiyama1994]					
		• SC258: Very poor reactivity with gp120 molecules outside of clade B [Moore1994b]					
		• SC258: Does not compete with IgG1b12 – reciprocal inhibition with MAbs L39, L40, and L78 [Ditzel1995]					
		• SC258: Several MAbs binding to various gp120 epitopes enhance binding, but the only MAb that SC258 enhanced binding of was anti-CD4 binding site MAb F91 – reciprocal inhibition with V2 region antibodies [Moore1996]					
		• SC258: Does not inhibit gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study – listed as not neutralizing [Trkola1996a]					
		• SC258: Transgenic mice carrying human genes allowing production of fully human MAbs were used to rapidly create a panel of anti-HIV gp120 MAb producing hybridomas by immunization with HIV SF162 gp120 – the previously described human MAbs 5145A(CD4BS) , 4117C (plus others, V3) and 697D (and SC258, V2) were used as controls [He2002]					
1002	L25	Env	gp120		L (weak)	HIV-1 infection	human (IgG1)
		Ab type V2-CD4BS					
		References Ditzel1995, Ditzel1997, Parren1997c					
		• L25: gp120 immobilized on solid phase by capture with anti-CD4 BS MAb L72 was used for selection of Fabs – a single anti-V2-CD4 BS Fab was obtained with with sensitivity to substitutions in the V2 and CD4 BS regions – rodent anti-V2 MAb SC258 competes with L25 [Ditzel1997]					
		• L25: Neutralizes TCLA strains weakly, but not primary isolates [Parren1997c]					
1003	L39	Env	gp120		no	HIV-1 infection	human (IgG1κ)
		Ab type V2-CD4BS					
		References Ditzel1995					
		• L39: This Fab does not inhibit sCD4 binding, but is inhibited by sCD4, probably due to conformational changes – it is competed by anti-V2 MAbs, and sensitive to amino acid substitutions in the V3 loop (similar patterns were observed for L39 and L78 gp120 amino acid substitutions enhancing or reducing binding) – does not compete with CD4BS MAbs, but is sensitive to amino acid changes at positions 368 and 370 – binding unaffected by deglycosylation – reciprocal inhibition with V2 MAbs SC258 and 684-238 – heavy and light chain variable region sequence is available [Ditzel1995]					
1004	L40	Env	gp120		no	HIV-1 infection	human (IgG1κ)
		Ab type V2-CD4BS					
		References Ditzel1995					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• L40: This Fab does not inhibit sCD4 binding, but is inhibited by sCD4, probably due to conformational changes – it is competed by anti-V2 MAbs, and sensitive to amino acid substitutions in the V3 loop (similar patterns were observed for L40 and L78 gp120 amino acid substitutions enhancing or reducing binding) – does not compete with CD4BS MAbs, but is sensitive to amino acid changes at positions 368 and 370 – binding only partially affected by deglycosylation – reciprocal inhibition with V2 MAbs SC258 and 684-238 – heavy and light chain variable region sequence is available [Ditzel1995]					
1005	L78	Env	gp120		L	HIV-1 infection	human (IgG1κ)
		Ab type V2-CD4BS **References** Ditzel1995 • L78: Substitutions at V2: (152/153 GE/SM, 183/184 PI/SG, 191/193 YL/GS), 262 N/T, V3 (314 G/W), CD4BS (257 T/R, 368 D/R, 370 E/R) inhibit binding, and some C4 and C5 substitutions enhance binding – this Fab does not inhibit sCD4 binding, but is inhibited by sCD4, probably due to conformational changes – it is competed by anti-V2 MAbs, and sensitive to amino acid substitutions in the V3 loop – does not compete with CD4BS MAbs, but is sensitive to amino acid changes at positions 368 and 370 – Fab neutralizes MN and LAI – binding unaffected by deglycosylation – reciprocal inhibition with V2 MAbs SC258 and 684-238 – heavy and light chain variable region sequence is available [Ditzel1995]					
1006		Env	gp120			HIV-1 infection	human
		Ab type V3 **References** Gilljam1999 • Sera from individuals with infections of HIV-1 subtype A-E were tested against purifed proteins from primary PBMC cultures. Sera reactivity tended not to be strongly related to subtype, rather probably reflected the sum of reactivities to conserved and variable regions in the proteins. V3 peptide comparisons showed some preference for within subtype binding [Gilljam1999].					
1007	110.J	Env	gp120				
		Ab type V3 **Donor** F. Traincard, Pasteur Institute, France **References** Thali1993, Moore1996 • 110.J: Inhibits sCD4-inducible anti-CD4 binding site MAb 48d [Thali1993] • 110.J: Binds to carboxy-terminal side of the V3 loop – reciprocal binding inhibition with other anti-V3 and anti-C4 MAbs – and reciprocal enhanced binding of some anti-V2 MAbs and anti-CD4 binding site MAbs [Moore1996]					
1008	1334-D (1334, 1334D)	Env	gp120 (HIV451)	TRTSV		HIV-1 infection	human (IgG1κ)
		Ab type V3 **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center) **References** Zolla-Pazner1999a, Zolla-Pazner1999b, Gorny2000a, Nyambi2000 • 1334-D: This MAb was selected on oligomeric gp160 from HIV451 [Zolla-Pazner1999a] • 1334-D: MAb peptide-reactivity pattern clustered with immunological related MAbs: 1334, 419, 504, 447, 453 and 537 – the core amino acids GP tended to be critical for reactivity in this group [Zolla-Pazner1999b] • 1334-D: Called 1334 – binds to V3 peptides from MN, SF2, NY5, RF, and CDC4 strains as well as x-reactivity with peptides from A, C, D, F, G, and H subtypes – was suggested to be IgG1lambda here – binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – V3 MAbs 447-52D, 838-D, and 1334 bound with a 7-10 fold preference for the oligomer [Gorny2000a] • 1334-D: Called 1334D – A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 1334D showed intermediate cross-reactivity [Nyambi2000]					
1009	2182	Env	(JRCSF)		P	HIV-1 infection	human (IgG1λ)
		Ab type V3 **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

References Gorny2002

- 2182: Conformation-dependent anti-V3 loop Abs may be more cross-reactive, so six new V3 MAbs were generated from cells of asymptomatic HIV-1-infected individuals by selection of heterhybridomas using a V3-fusion protein (V3-fp), the HIV-1 JRCSF V3 loop inserted into a truncated murine leukemia virus gp70 – the six new MAbs all bind to the tip of the V3 loop and cross-compete with the MAb 447-52D and are conformationally sensitive – MAbs showed cross-clade binding to native, intact virions of clades A(N=2), B(N=4), and F(N=2), limited binding to C(N=3) and D(N=3), and did not bind to CRF01(subtype E, N=2) – the strength binding was highly correlated with percent neutralization using the ghost cell or PHA blast assay – five well-characterized MAbs were used as controls: anti-V3 447-52D (anti-V3 MAb for competition and neutralization studies), 654 (anti-CD4BS used as a conformation-sensitive MAb control), 1331A (anti-C5 used as a linear binding site MAb control), MAb 246 (anti-gp41 MAb that bound to primary isolates of all clades) – 5/6 MAbs were derived from individuals infected in the US, presumably with clade B, and one, 2182, was derived from an individual who was infected abroad with clade A who is presently living in New York city – 2412 and 2456 were produced from cells obtained from the same individual, while the other MAbs were each generated from different subjects – 2182 bound to 8/16 of the diverse isolates, not to any clade C or CRF01 [Gorny2002]

1010	2191	Env	(JRCSF)		P	HIV-1 infection	human (IgG1λ)

Ab type V3 **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny2002

- 2191: Conformation-dependent anti-V3 loop Abs may be more cross-reactive, so six new V3 MAbs were generated from cells of asymptomatic HIV-1-infected individuals by selection of heterhybridomas using a V3-fusion protein (V3-fp), the HIV-1 JRCSF V3 loop inserted into a truncated murine leukemia virus gp70 – the six new MAbs all bind to the tip of the V3 loop and cross-compete with the MAb 447-52D and are conformationally sensitive – MAbs showed cross-clade binding to native, intact virions of clades A(N=2), B(N=4), and F(N=2), limited binding to C(N=3) and D(N=3), and did not bind to CRF01(subtype E, N=2) – the strength binding was highly correlated with percent neutralization using the ghost cell or PHA blast assay – five well-characterized MAbs were used as controls: anti-V3 447-52D (anti-V3 MAb for competition and neutralization studies), 654 (anti-CD4BS used as a conformation-sensitive MAb control), 1331A (anti-C5 used as a linear binding site MAb control), MAb 246 (anti-gp41 MAb that bound to primary isolates of all clades) – 5/6 MAbs were derived from individuals infected in the US, presumably with clade B, and one, 2182, was derived from an individual who was infected abroad with clade A who is presently living in New York city – 2412 and 2456 were produced from cells obtained from the same individual, while the other MAbs were each generated from different subjects – 2191 bound to 10/16 of the diverse isolates, not to any clade D or CRF01 [Gorny2002]

1011	2219	Env	(JRCSF)		P	HIV-1 infection	human (IgG1λ)

Ab type V3 **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny2002

- 2219: Conformation-dependent anti-V3 loop Abs may be more cross-reactive, so six new V3 MAbs were generated from cells of asymptomatic HIV-1-infected individuals by selection of heterhybridomas using a V3-fusion protein (V3-fp), the HIV-1 JRCSF V3 loop inserted into a truncated murine leukemia virus gp70 – the six new MAbs all bind to the tip of the V3 loop and cross-compete with the MAb 447-52D and are conformationally sensitive – MAbs showed cross-clade binding to native, intact virions of clades A(N=2), B(N=4), and F(N=2), limited binding to C(N=3) and D(N=3), and did not bind to CRF01(subtype E, N=2) – the strength binding was highly correlated with percent neutralization using the ghost cell or PHA blast assay – five well-characterized MAbs were used as controls: anti-V3 447-52D (anti-V3 MAb for competition and neutralization studies), 654 (anti-CD4BS used as a conformation-sensitive MAb control), 1331A (anti-C5 used as a linear binding site MAb control), MAb 246 (anti-gp41 MAb that bound to primary isolates of all clades) – 5/6 MAbs were derived from individuals infected in the US, presumably with clade B, and one, 2182, was derived from an individual who was infected abroad with clade A who is presently living in New York city – 2412 and 2456 were produced from cells obtained from the same individual, while the other MAbs were each generated from different subjects – 2219 bound to 13/16 of the diverse isolates [Gorny2002]

1012	2412	Env	(JRCSF)		P	HIV-1 infection	human (IgG1λ)

Ab type V3 **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny2002

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 2412: Conformation-dependent anti-V3 loop Abs may be more cross-reactive, so six new V3 MAbs were generated from cells of asymptomatic HIV-1-infected individuals by selection of heterhybridomas using a V3-fusion protein (V3-fp), the HIV-1 JRCSF V3 loop inserted into a truncated murine leukemia virus gp70 – the six new MAbs all bind to the tip of the V3 loop and cross-compete with the MAb 447-52D and are conformationally sensitive – MAbs showed cross-clade binding to native, intact virions of clades A(N=2), B(N=4), and F(N=2), limited binding to C(N=3) and D(N=3), and did not bind to CRF01(subtype E, N=2) – the strength binding was highly correlated with percent neutralization using the ghost cell or PHA blast assay – five well-characterized MAbs were used as controls: anti-V3 447-52D (anti-V3 MAb for competition and neutralization studies), 654 (anti-CD4BS used as a conformation-sensitive MAb control), 1331A (anti-C5 used as a linear binding site MAb control), MAb 246 (anti-gp41 MAb that bound to primary isolates of all clades) – 5/6 MAbs were derived from individuals infected in the US, presumably with clade B, and one, 2182, was derived from an individual who was infected abroad with clade A who is presently living in New York city – 2412 and 2456 were produced from cells obtained from the same individual, while the other MAbs were each generated from different subjects – 2412 bound to 7/16 of the diverse isolates, and did not bind to any of the clade C, D or CRF01 viruses [Gorny2002]			
1013	2442	Env	(JRCSF)		P	HIV-1 infection	human (IgG1λ)
		Ab type V3 **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center) **References** Gorny2002					
		• 2442: Conformation-dependent anti-V3 loop Abs may be more cross-reactive, so six new V3 MAbs were generated from cells of asymptomatic HIV-1-infected individuals by selection of heterhybridomas using a V3-fusion protein (V3-fp), the HIV-1 JRCSF V3 loop inserted into a truncated murine leukemia virus gp70 – the six new MAbs all bind to the tip of the V3 loop and cross-compete with the MAb 447-52D and are conformationally sensitive – MAbs showed cross-clade binding to native, intact virions of clades A(N=2), B(N=4), and F(N=2), limited binding to C(N=3) and D(N=3), and did not bind to CRF01(subtype E, N=2) – the strength binding was highly correlated with percent neutralization using the ghost cell or PHA blast assay – five well-characterized MAbs were used as controls: anti-V3 447-52D (anti-V3 MAb for competition and neutralization studies), 654 (anti-CD4BS used as a conformation-sensitive MAb control), 1331A (anti-C5 used as a linear binding site MAb control), MAb 246 (anti-gp41 MAb that bound to primary isolates of all clades) – 5/6 MAbs were derived from individuals infected in the US, presumably with clade B, and one, 2182, was derived from an individual who was infected abroad with clade A who is presently living in New York city – 2412 and 2456 were produced from cells obtained from the same individual, while the other MAbs were each generated from different subjects – 2442 bound to 13/16 of the diverse isolates [Gorny2002]			
1014	2456	Env	(JRCSF)		P	HIV-1 infection	human (IgG1λ)
		Ab type V3 **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center) **References** Gorny2002					
		• 2456: Conformation-dependent anti-V3 loop Abs may be more cross-reactive, so six new V3 MAbs were generated from cells of asymptomatic HIV-1-infected individuals by selection of heterhybridomas using a V3-fusion protein (V3-fp), the HIV-1 JRCSF V3 loop inserted into a truncated murine leukemia virus gp70 – the six new MAbs all bind to the tip of the V3 loop and cross-compete with the MAb 447-52D and are conformationally sensitive – MAbs showed cross-clade binding to native, intact virions of clades A(N=2), B(N=4), and F(N=2), limited binding to C(N=3) and D(N=3), and did not bind to CRF01(subtype E, N=2) – the strength binding was highly correlated with percent neutralization using the ghost cell or PHA blast assay – five well-characterized MAbs were used as controls: anti-V3 447-52D (anti-V3 MAb for competition and neutralization studies), 654 (anti-CD4BS used as a conformation-sensitive MAb control), 1331A (anti-C5 used as a linear binding site MAb control), MAb 246 (anti-gp41 MAb that bound to primary isolates of all clades) – 5/6 MAbs were derived from individuals infected in the US, presumably with clade B, and one, 2182, was derived from an individual who was infected abroad with clade A who is presently living in New York city – 2412 and 2456 were produced from cells obtained from the same individual, while the other MAbs were each generated from different subjects – 2456 bound to 12/16 of the diverse isolates [Gorny2002]			
1015	39F	Env	gp120		no		
		Ab type V3 **Donor** James Robinson, Tulane University, New Orleans, LA, USA **References** Yang2002, Grundner2002					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 39F: Uncleaved soluble gp140 (YU2 strain, R5 primary isolate) can be stabilized in an oligomer by fusion with a C-term trimeric GCN4 motif or using a T4 trimeric motif derived from T4 bacteriophage fibritin – stabilized oligomer gp140 delta683(-FT) showed strong preferential recognition by NAbs IgG1b12 and 2G12 relative to the gp120 monomer, in contrast to poorly neutralizing MAbs F105, F91, 17b, 48d, and 39F which showed reduced levels of binding, and C11, A32, and 30D which did not bind the stabilized oligomer [Yang2002] • 39F: HIV-1 gp160deltaCT (cytoplasmic tail-deleted) proteoliposomes (PLs) containing native, trimeric envelope glycoproteins from R5 strains YU2 and JRFL, and X4 strain HXBc2, were made in a physiologic membrane setting as candidate immunogens for HIV vaccines – 2F5 bound to gp160deltaCT with a reconstituted membrane ten-fold better than the same protein on beads – anti-CD4BS MAbs IgG1b12 and F105, A32 (C1-C4), C11 (C1-C5), and 39F (V3) MAbs bound gp160deltaCT PLs indistinguishably from gp160deltaCT expressed on the cell surface [Grundner2002]			
1016	55/68b	Env	gp120 (300–315)				
		Ab type V3 **References** Peet1998 • 55/68b: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind, and anti-V3 MAb 55/68b binding was abrogated by V3 serine substitutions in the V3 loop – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions [Peet1998]					
1017	5G11	Env	gp120				
		Ab type V3 **Donor** S. Nigida and L. Arthur, NCI, Frederick, MD USA **References** Moore1996 • 5G11: Binds to conformation sensitive epitope in the V3 loop – reciprocal inhibition of other V3 loop MAbs – reciprocal enhancement of some C1-C5 MAbs (unusual for an anti-V3 MAb) and CD4 binding site MAbs – and enhances binding of V2 MAbs [Moore1996]					
1018	6.1	Env	gp120 (SF162)		no	Vaccine	human from transgenic mice (IgG2κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) **Ab type** V3 **Donor** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** He2002 • 6.1: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – 3/4 V3 MAbs bound a similar linear epitope between positions 11-30 of the MN V3 loop (8E11/A8, 6.1, and 6.7), but only 8E11/A8 could weakly neutralize autologous strain SF162 [He2002]					
1019	6.7	Env	gp120 (SF162)		no	Vaccine	human from transgenic mice (IgG2κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) **Ab type** V3 **Donor** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** He2002 • 6.7: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – 3/4 V3 MAbs bound a similar linear epitope between positions 11-30 of the MN V3 loop (8E11/A8, 6.1, and 6.7), but only 8E11/A8 could weakly neutralize autologous strain SF162 [He2002]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
1020	8.27.3	Env	gp120 (SF162)		L	Vaccine	human from transgenic mice (IgG2κ)

Vaccine *Vector/Type:* recombinant protein *Strain:* SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM)
Ab type V3 **Donor** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References He2002

- 8.27.3: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – 1/4 V3 MAbs, 8.27.3, bound a discontinuous epitope that was broadly cross-reactive with B clade R5 and X4 strains (not E clade) and could neutralize autologous strain SF162 [He2002]

1021	8E11/A8	Env	gp120 (SF162)		L	Vaccine	human from transgenic mice (IgG2κ)

Vaccine *Vector/Type:* recombinant protein *Strain:* SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM)
Ab type V3 **Donor** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References He2002

- 8E11/A8: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – 3/4 V3 MAbs bound a similar linear epitope between positions 11-30 of the MN V3 loop (8E11/A8, 6.1, and 6.7), but only 8E11/A8 could weakly neutralize autologous strain SF162 [He2002]

1022	9305	Env	gp120		L		murine

Ab type V3 **Donor** Du Pont, Wilmington DE
References McDougal1996

1023	AG1121 (1121)	Env	gp120		L		

Ab type V3 **Donor** AGMED, Inc, Bedford, MA, USA or ImmunoDiagnostics, Inc, Woburn, MA, USA
References Sullivan1995, Cao1997b, Si2001

- AG1121: Recognizes monomeric gp120 from T-cell adapted line HXBc2 and primary isolate 89.6 equally well, but 89.6 was three-fold less sensitive to neutralization by AG1121 than HXBc2 [Sullivan1995]
- AG1121: Called 1121 – Virus with the V1-V2 loop deleted was viable and more susceptible to neutralization by CD4i MAb 17b, and anti-V3 MAbs 1121, 9284, and 110.4, but not to and CD4BS MAb F105 or sCD4 [Cao1997b]
- AG1121: SHIV-HXBc2 is a neutralization sensitive non-pathogenic virus, and several in vivo passages through monkey's yielded highly pathogenic SHIV KU-1 – HXBc2 and the KU-1 clone HXBc2P3.2 differ in 12 amino acids in gp160 – substitutions in both gp120 and gp41 reduced the ability of sCD4, IgG1b12, F105 and AG1121 to Env achieve saturation and full occupancy, and neutralize KU-1 – 17b and 2F5 also bound less efficiently to HXBc2P3.2, although 2G12 was able to bind both comparably [Si2001]

1024	D47	Env	gp120 (IIIB)			Vaccine	murine

Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* Env
Ab type V3 **Donor** Patricia Earl, NIAID, NIH
References Earl1994, Richardson1996, Otteken1996, Wyatt1997, Earl1997, Salzwedel2000

- D47: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response [Earl1994]
- D47: Used for capture of oligomeric Env for antigen capture ELISA – binding of this antibody to oligomeric Env IIIB was not blocked by human sera from the US, consistent with a low prevalence of IIIB-like V3 strains [Richardson1996]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• D47: Pulse label experiments of MAb binding to noncleavable gp160 revealed that this anti-V3 MAb bound immediately and binding stayed constant through chase period [Otteken1996] • D47: Binds both gp120 and soluble gp120+gp41 complex efficiently, suggesting its gp120 epitope is not blocked by gp41 binding [Wyatt1997] • D47: Used for comparison in a study of gp41 antibodies – D47 binds to a greater extent to cell surface expressed Env than any of 38 conformation dependent anti-gp41 MAbs [Earl1997] • D47: sCD4 can activate fusion between effector cells expressing Env and target cells expressing coreceptor (CCR5 or CXCR4) alone without CD4 – V3 MAb D47 is strain specific and can inhibit sCD4 mediated infection, but only of the closely related LAV Env, while anti-CD4i MAbs were broadly cross-neutralizing [Salzwedel2000]				
1025	F5.5	Env	gp120 (IIIB)				murine
		Ab type V3 **Donor** Hybridolabs, Institute Pasteur **References** Altmeyer1999 • F5.5: A Semliki Forest virus (SFV) expression system carrying BX08 env was used to study the conformation of gp120 Env – intracytoplasmic gp120 was recognized by the anti-V3 MAbs K24 and F5.5, while gp120 at the plasma membrane was detected only by conformation dependent MAbs 2G12, 670-D and 694/98D and not V3 MAbs – expression in rat brain also showed that surface-expressed Env was recognized only by the conformation-dependent antibodies and not by anti-V3 antibodies [Altmeyer1999]				
1026	G3-1472	Env	gp120				
		Ab type V3 **Donor** M. Fung **References** Moore1996 • G3-1472: Binds to carboxy-terminal side of the V3 loop – reciprocal binding inhibition with other anti-V3 and anti-C4 MAbs – reciprocal enhanced binding of some anti-V2 MAbs and anti-CD4 binding site MAbs – binding inhibited by anti-C4 MAbs [Moore1996]				
1027	K24	Env	gp120 (IIIB)				murine
		Ab type V3 **Donor** Hybridolabs, Institute Pasteur **References** Altmeyer1999 • K24: A Semliki Forest virus (SFV) expression system carrying BX08 env was used to study the conformation of gp120 env – intracytoplasmic gp120 was recognized by the anti-V3 MAbs K24 and F5.5, while gp120 at the plasma membrane was detected only by conformation dependent MAbs 2G12, 670-D and 694/98D and not V3 MAbs – expression in rat brain also showed that surface-expressed Env was recognized only by the conformation-dependent antibodies and not by anti-V3 antibodies [Altmeyer1999]				
1028	TH1	Env	gp120		L (MN, JRCSF)		human (IgG1λ)
		Ab type V3 **Donor** Michael Fung, Tanox Biosystem, USA **References** D'Souza1995, Yang1998 • TH1: Found to neutralize MN and JRCSF, but not two B subtype primary isolates, nor a D subtype primary isolate, by most labs in a multi-laboratory study involving 11 labs [D'Souza1995] • TH1: A neutralization assay was developed based on hemi-nested PCR amplification of the LTR (HNPCR) – LTR-HNPCR consistently revealed HIV DNA and was shown to be a rapid, specific and reliable neutralization assay based on tests with 6 MAbs and 5 isolates [Yang1998]				
1029	anti-gp120/V3	Env	gp120			Vaccine	murine (IgG)
		Vaccine *Vector/Type:* recombinant protein, virus-like particle *Strain:* A clade 94UG018 *HIV component:* Gag, Pol, Nef, gp120 **Ab type** V3 **Donor** Intracel Co **References** Buonaguro2001					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• Anti-V3: HIV-1 pr55 gag-based virus-like particles (VLP) carrying Nef and Pol open reading frames as well as gp120 of the clade A isolate 94UG018 were created using a Baculovirus expression system to package additional ORFS into the VLP – anti-V3 and anti-p24 antibodies were used to assess the expression levels and Gag and gp120-TM were found to be expressed at comparable levels on the VLP [Buonaguro2001]					
1030	polyclonal	Env	gp120		no	Vaccine	murine
		Vaccine *Vector/Type:* recombinant protein, virus-like particle *Strain:* LAI *HIV component:* V3, CD4BS, p55 **Ab type** V3 **References** Truong1996					
		• Antibodies raised against recombinant anti-p55 virus-like particles with the p24 region 196-226 deleted, bearing inserts of either the V3 or the CD4BS regions of gp120 were studied – no neutralizing responses, weak Env, and strong Gag responses were elicited – the major homology region (MHR) and proximal sequences was found to be required for capsid assembly [Truong1996]					
1031	polyclonal	Env	gp120		yes	Vaccine	human
		Vaccine *Vector/Type:* canarypox prime with recombinant protein boost *Strain:* MN, SF2, LAI *HIV component:* gp120 MN, gp41 LAI, Gag LAI, partial Pol LAI, rgp120 SF2 *Adjuvant:* MF-59 **Ab type** V3 **References** Verrier2000					
		• Serum Abs elicited by this vaccine reacted with V3 peptides from clades B, C, and F, reacted weakly with V3 peptides from clades A, D, G, and H, and did not react with V3 peptides from clades E and O – neutralizing activity against 5 of 14 primary isolates tested was observed, including one B clade X4 virus, two dualtropic B clade viruses (from clade B) and one clade B and one clade C R5 virus [Verrier2000]					
1032	polyclonal	Env	gp120 (303–325)		no	in vitro stimulation	human (IgM)
		Ab type V3 **References** Sidorova1999					
		• Polyspecific anti-MN-24 antibodies were raised through V3 peptide, MN-24 stimulation of human cells, followed by EBV transformation: they react with homologous and heterologous peptides and may be autoantibodies [Sidorova1999]					
1033	polyclonal	Env					human
		Ab type V3 **References** Guevara2002					
		• Viral RNA in serum and high titers of subtype C consensus V3 peptide binding Abs were the best independent predictors of mother to infant transmission of HIV-1 subtype C – NAb to subtype B HIV-1(MN) was also correlated [Guevara2002]					
1034	polyclonal	Env			L	Vaccine	murine (IgA)
		Vaccine *Vector/Type:* HIV-1 captured on concavalin A-immobilized polystyrene nanospheres, Con A-NS *Strain:* IIIB *HIV component:* heat-inactivated virus, gp120 *Adjuvant:* concavalin A-immobilized polystyrene nanospheres **Ab type** V3 **References** Kawamura2002					
		• Vaginal fluids were collected after intravaginal immunization of BALB/c mice and analyzed for their anti-HIV-1 antibody levels using a IIIB-V3 ELISA and IIIB neutralization assay – HIV-1 specific IgG was undetectable but anti-HIV IgA antibody response was identified in the vaginal fluids of immunized mice with HIV concavalin A-immobilized polystyrene nanosheres [Kawamura2002]					
1035	polyclonal	Env			L	Vaccine	human (IgG1, IgG2a, IgA)
		Vaccine *Vector/Type:* peptide *Strain:* MN, 89.6P *HIV component:* C4-V3 *Adjuvant:* IL-1alpha, IL-12, and IL-18 or GM-CSF, or cholera toxin, alum					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		Ab type V3 **References** Bradney2002 • The cytokine-adjuvant combination IL-1alpha, IL-12 and IL-18 were found to stimulate potent mucosal antibody responses upon intranasal immunization of mice – cholera toxin is the most widely used adjuvant, but is not safe for use in humans [Bradney2002]					
1036	polyclonal	Env				Vaccine	murine
		Vaccine *Vector/Type:* peptide *Strain:* multiple epitope immunogen *HIV component:* V3 *Adjuvant:* Freund's adjuvant **Ab type** V3 **References** Hewer2002 • A synthetic peptide immunogen designated a multiple epitope immmunogen (MEI) was generated by synthesizing peptides with mixtures of frequently found amino acids (>10%) from the C subtypes allowed in the synthetic peptide – when injected into mice, the C subtype MEI induced antibodies that recognized the immunogen and whole virus as an antigen in ELIZAs – sera from eight HIV positive South Africans recognized the MEI peptide in ELISA tests [Hewer2002]					
1037	11/75a/21/41	Env	gp120				
		Ab type V3 discontinuous **References** McKeating1992a, Peet1998 • 11/75a/21/41: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind, but anti-V3 MAb 11/75a/21/41 binding was dramatically diminished by V3 serine substitutions – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions [Peet1998]					
1038	41.1 (ICR41.1i, ICR41)	Env	gp120 (HXB10)		L (HXB2)	Vaccine	rat (IgG2a)
		Vaccine *Vector/Type:* recombinant protein *Strain:* BH10 *HIV component:* gp120 **Ab type** V3 discontinuous **Donor** J. Cordell, Institute for Cancer Research, Sutton, Surrey, UK **References** McKeating1992a, McKeating1993b, Klasse1993a, McLain1994, Armstrong1996a, Armstrong1996b, Jeffs1996, Ugolini1997 • 41.1: The gp41 mutation 582(Ala to Thr) results in conformational changes in gp120 that confer neutralization resistance to conformationally sensitive neutralizing MAbs – neutralization efficiency of 41.1 is not affected [Reitz1988, Klasse1993a] • 41.1: Called ICR41.1i – Kinetics of neutralization studied – no lag for 39.3b, while ICR 39.13g and ICR 41.1i have lags of 5 and 15 min respectively – neutralization mediated by 3 molecules of IgG per virion – most efficient at neutralization of the three MAbs studied – acts with multi-hit kinetics [McLain1994] • 41.1: Called ICR41.1i – IgG2c? – Neutralization was affected if the Ab was added after the virus bound to the host cells at 24 degrees C or below [Armstrong1996a] • 41.1: Called ICR41.1i – Neutralization occurs by blocking a post-fusion internalization event, in contrast to MAb F58 [Armstrong1996b] • 41.1: Deletion of the V1V2 regions did not affect anti-V3 Abs ability to bind when compared to intact rec gp120 [Jeffs1996] • 41.1: Viral binding inhibition by 41.1 was weakly correlated with neutralization (all other neutralizing MAbs tested showed some correlation except 2F5) [Ugolini1997]					
1039	55/45a/1l	Env	gp120				
		Ab type V3 discontinuous **References** Peet1998					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 55/45a/11: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind, and anti-V3 MAb 55/45a/11 binding was only marginally diminished by V3 serine substitutions – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions [Peet1998]					
1040	1108	Env	Env			HIV-1 infection	human (IgG1λ)
		Ab type V3 mimotope **References** Zolla-Pazner1999a, Zolla-Pazner1999b • 1108: Selected with peptide 987, a mimotope of anti-V3 MAb 447-D – MAb peptide reactivity pattern clustered with immunological related MAbs: 1108, 386, 268, 311, 257, 694.8 – the amino acids HI tended to be critical for reactivity in this group [Zolla-Pazner1999b] • 1108: The sequence of peptide 987, used to select MAb 1108, is ADGAWRSVHLGPGRGSGSGMGK [Zolla-Pazner1999a]					
1041	polyclonal	Env				HIV-1 infection	human (IgA, IgG)
		Ab type V3, V4 **References** Skott1999 • IgA and IgG from 45 HIV+ individuals was studied – people with low CD4+ cell counts had decreased levels IgA in saliva – sera and saliva IgA was primarily directed toward Env – peptide ELISA studies indicated that teh dominant IgA eptiopes were the V4 region (aa 385-409) and the C-term part of the V3 loop (aa 325-344), while the IgG response was directed towards the tip of the loop (aa 308-325) [Skott1999]					
1042	polyclonal	Env	gp120 (IIIB)			Vaccine	rabbit
		Vaccine *Vector/Type:* peptide *Strain:* MN *HIV component:* gp120 V3/C4 *Adjuvant:* mucosal adjuvant CT **Ab type** V3-C4 **References** Zinckgraf1999 • Nasal mucosal immunization and boosting of HIV peptide and was superior for inducing serum IgG and vaginal secretory IgA compared to nasal immunization and vaginal boosting – vaginal immunization and boosting resulted low serum IgG and vaginal IgA and a high vaginal IgG response [Zinckgraf1999]					
1043	D27	Env	gp120 (IIIB)			Vaccine	murine (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140 **Ab type** V3-CD4BS **Donor** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD **References** Earl1994, Otteken1996, Sugiura1999 • D27: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response [Earl1994] • D27: Pulse label experiments of 4 MAbs (D20, D27, T20, and T22) binding to noncleavable gp160 revealed that these anti-CD4 MAbs bound with a delay, and that the epitope formed with a t 1/2 of about 10 minutes [Otteken1996] • D27: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D27 is one of two MAbs labeled group Ca, that was type-specific for BH8 – D27 fully blocked CD4 binding, and the deletion of the V3 loop abrogated binding [Sugiura1999]					
1044	D56	Env	gp120 (IIIB)		L	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140 **Ab type** V3-CD4BS **Donor** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD **References** Earl1994, Sugiura1999 • D56: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response [Earl1994]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- D56: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D56 is one of two MAbs labeled group Ca, that was type-specific for BH8 – D56 fully blocked CD4 binding, and the deletion of the V3 loop abrogated binding – 12.5 ug/ml of D56 was required to achieve 50% neutralization of HIV-1 NL4-3 [Sugiura1999]

1045 2G12 (c2G12) Env gp120 L P HIV-1 infection human (IgG1κ)

Ab type carbohydrates at glycosylation residues in C2, C3, C4, and V4 **Donor** Herman Katinger, Inst. Appl. Microbiol. or Polymun Scientific Inc., Vienna, Austria, MRC AIDS reagent project

References Buchacher1994, Trkola1995, Moore1995b, McKeating1996b, McKeating1996a, Trkola1996b, Moore1996, Poignard1996b, Trkola1996a, Sattentau1996, D'Souza1997, Mo1997, Binley1997a, Fouts1997, Li1997, Moore1997, Mascola1997, Ugolini1997, Burton1997, Parren1997c, Andrus1998, Wyatt1998a, Mondor1998, Parren1998a, Sullivan1998b, Connor1998, Binley1998, Trkola1998, Fouts1998, Takefman1998, Parren1998b, Li1998, Wyatt1998b, Frankel1998, Kunert1998, Schonning1998, Montefiori1999, Beddows1999, Altmeyer1999, Poignard1999, Parren1999, Mascola1999, Mascola2000, Binley1999, Robert-Guroff2000, Baba2000, Grovit-Ferbas2000, Park2000, Si2001, Mascola2001, Zwick2001c, Barnett2001, Moore2001, Poignard2001, Zeder-Lutz2001, Verrier2001, Stiegler2001, Spenlehauer2001, Hofmann-Lehmann2001, Xu2001, Savarino2001, Golding2002b, Sanders2002, Scanlan2002, Schulke2002, Yang2002, Xu2002, Chakrabarti2002, Armbruster2002, Edwards2002, Grundner2002, Mascola2002, Zhang2002, Ferrantelli2002, Liu2002, Pantophlet2003, Herrera2003

- 2G12: Human MAb generated by electrofusion of PBL from HIV-1+ volunteers with CB-F7 cells [Buchacher1994]
- 2G12: Highly potent Cross-clade neutralizing activity [Trkola1995]
- 2G12: Conformationally sensitive epitope destroyed by mutations altering the N-linked glycosylation sites near the base of the V3 loop and the amino-terminal flank of the V4 loop [Trkola1996b]
- 2G12: Binding weakly enhanced by some anti-C1, -C4, -V3, and CD4 binding site MAbs – unusual in that 2G12 binding neither enhanced or inhibited the binding of other MAbs included in the study [Moore1996]
- 2G12: Review: binding site is distinct from CD4BS MAbs epitope and is unique among known gp120 MAbs, human or rodent [Moore1995b]
- 2G12: Review: exceptional capacity to neutralize primary isolates in terms of both breadth and potency – one of three MAbs (IgG1b12, 2G12, and 2F5) generally accepted as having significant potency against primary isolates [Poignard1996b]
- 2G12: Neutralizes JR-FL – inhibits gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study [Trkola1996a]
- 2G12: Neutralizes primary isolates, HXB2, and chimeric virus with gp120 from primary isolates in an HXB2 background [McKeating1996b]
- 2G12: Review: Only four epitopes have been described which can stimulate a useful neutralizing response to a broad spectrum of primary isolates, represented by the binding sites of MAbs: 447-52-D, 2G12, Fab b12, and 2F5 [Sattentau1996]
- 2G12: In a multilab evaluation of monoclonal antibodies, only IgG1b12, 2G12, and 2F5 could neutralize at least half of the 9 primary test isolates at a concentration of < 25 mug per ml for 90% viral inhibition – neutralized 6 of 9 primary isolates [D'Souza1997]
- 2G12: A JRCSF variant that was selected for IgG1b12 resistance remained sensitive to MAbs 2G12 and 2F5, for combination therapy [Mo1997]
- 2G12: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric Env binding – 2G12 bound monomer, and weakly bound oligomer and neutralized JRFL [Fouts1997]
- 2G12: One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB Env – 2G12 was a strong neutralizer of SHIV-vpu+ – all Ab combinations tested showed synergistic neutralization – 2G12 has synergistic response with MAbs 694/98-D (anti-V3), 2F5, F105, and b12 [Li1997]
- 2G12: Review: MAbs 2F5, 2G12 and IgG1b12 have potential for use in combination with CD4-IgG2 as an immunotherapeutic or immunoprophylactic – homologous MAbs to these are rare in humans and vaccine strategies should consider including constructs that may enhance exposure of these MAbs' epitopes [Moore1997]
- 2G12: Using concentrations of Abs achievable in vivo, the triple combination of 2F5, 2G12 and HIVIG was found to be synergistic to have the greatest breadth and magnitude of response against 15 clade B primary isolates [Mascola1997]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 2G12: Viral binding inhibition by 2G12 was strongly correlated with neutralization (all other neutralizing MAbs tested showed some correlation except 2F5) [Ugolini1997]
- 2G12: Review that discusses this MAb – reacts with residues at the base of the V3 loop and V4, and most of the changes that reduce binding are glycosylation sites – it is not clear whether the binding site is peptidic or direct carbohydrate [Burton1997]
- 2G12: Neutralizes TCLA strains and primary isolates [Parren1997c]
- 2G12: Post-exposure prophylaxis was effective when MAb 694/98-D was delivered 15 min post-exposure to HIV-1 LAI in hu-PBL-SCID mice, but declined to 50% if delivered 60 min post-exposure, and similar time constraints have been observed for HIVIG, 2F5 and 2G12, in contrast to MAb BAT123 that could protect delivered 4 hours post infection [Andrus1998]
- 2G12: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren1998a]
- 2G12: Summary of the implications of the crystal structure of gp120 combined with what is known about mutations that reduce NAb binding – probable mechanism of neutralization by 2G12 is unknown, but dependent on proper glycosylation and 2G12 is predicted to be oriented toward the target cell when bound, so neutralization may be due to steric hindrance – mutations in positions N 295, T 297, S 334, N 386, N 392 and N 397 HXBc2 (IIIB) decrease 2G12 binding, and the binding region is 25 angstroms from the CD4 binding site – probably the Ab binds in part to carbohydrates, which may account for both its broad reactivity and the scarcity of Abs in the same competition group [Wyatt1998a]
- 2G12: Enhances Hx10 binding to CD4 positive or negative HeLa cells, but inhibited binding to CD4+ T-cell line A3.01 – neutralizes Hx10 infection of the HeLa cells [Mondor1998]
- 2G12: Ab from gp120 vaccinated individuals prior to infection, who subsequently became HIV infected, could not achieve 90% neutralization of the primary virus by which the individuals were ultimately infected – these viruses were not particularly refractive to neutralization, as determined by their susceptibility to neutralization by MAbs 2G12, IgG1b12, 2F5 and 447-52D [Connor1998]
- 2G12: Does not compete with binding of MAb generated in response to gp120-CD4 complex, CG10 [Sullivan1998b]
- 2G12: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer – MAb 2G12 was the only exception to this, showing reduced binding efficiency [Binley1998]
- 2G12: A wide range of neutralizing titers was observed that was independent of co-receptor usage [Trkola1998]
- 2G12: Notes that 2G12 and 2F5, potent neutralizing antibodies, were identified by screening for cell surface (oligomeric Envelope) reactivity [Fouts1998]
- 2G12: Induces Complement-mediated lysis in MN but not primary isolates – primary isolates are refractive to CML [Takefman1998]
- 2G12: MAbs 2G12, 2F5 and b12 are broadly neutralizing, as are some human polyconal sera, but this paper describes a set of primary isolates that are resistant to all three MAbs and 2 broadly neutralizing sera – results indicate that resistance levels of pediatric isolates might be higher than adult isolates – resistance in general did not seem to be conferred by a loss of binding affinity for gp120 or gp41, rather by a more global perturbation of oligomeric Envelope [Parren1998b]
- 2G12: Neutralization synergy was observed when the MAbs 694/98-D (V3), 2F5 (gp41), and 2G12 (gp120 discontinuous) were used in combination, and even greater neutralizing potential was seen with the addition of a fourth MAb, F105 (CD4 BS) [Li1998]
- 2G12: Discussed in a review of the antigenic and receptor binding-domains of gp120 in relation to the structure of the molecule – antibodies are discussed by category (anti-V2, anti-V3, CD4i, CD4BS...), however as 2G12 binds to a rarely immunogenic region, and it is dependent on glycosylation, it was discussed individually [Wyatt1998b]
- 2G12: The complete V, J and D(H) domain was sequenced – unlike non-neutralizing anti-gp41 MAb 3D6, five neutralizing MAbs (2F5, 2G12, 1B1, 1F7, and 3D5) showed extensive somatic mutations giving evidence of persistent antigenic pressure over long periods – 2G12 D(H) has the best homology to a D(H) segment between D3-22 and D4-23, a region not usually considered for heavy-chain rearrangement because it lacks associated recombination signals in the flanking regions, Kunert et al. suggest this may be why Abs that compete with 2G12 are rare [Kunert1998]
- 2G12: In a study of the influence of the glycan at position 306 of the V3 loop on MAb recognition, 2G12 was found to neutralize an HIV-BRU mutant virus that lacks the V3 loop glycan and has a mutation at the tip of the loop more efficiently than it neutralizes HIV-BRU [Schonning1998]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 2G12: Infection of dendritic cells cultured from CD14+ blood cells or from cadaveric human skin was blocked by neutralizing MAbs IgG1b12, or 2F5 and 2G12 delivered together, but not by control non-neutralizing anti-gp120 MAb 4.8D, indicating that NAbs could interrupt early mucosal transmission events [Frankel1998]
- 2G12: A meeting summary presented results regarding neutralization –MAbs 2G12 and 2F5 tested for their ability to neutralize primary isolate infection of genetically engineered cell lines (cMAGI and others, presented by T. Matthews, A. Trkola, J. Bradac) – an advantage of such cells lines over PBMCs is that markers (X-Gal) can be added for staining to simplify the assay – the consensus of the meeting was that these engineered cell lines did not improve the sensitivity of detection of primary isolate neutralization – D. Burton and J. Mascola presented results concerning passive immunization and protection of hu-PBL-SCID mice and macaques, respectively, and both found combinations of MAbs that were able to achieve 99% neutralization in vitro corresponded to efficacy in vivo [Montefiori1999]
- 2G12: rgp120 derived from a R5X4 subtype B virus was used to vaccinate healthy volunteers and the resulting sera were compared with sera from HIV-1 positive subjects and neutralizing MAbs – 2G12 was able to bind with low affinity to the rgp120 monomer HIV-1 W61D [Beddows1999]
- 2G12: A Semliki Forest virus (SFV) expression system carrying BX08 Env was used to study the conformation of gp120 Env – intracytoplasmic gp120 was recognized by the anti-V3 MAbs K24 and F5.5, while gp120 at the plasma membrane was detected only by conformation dependent MAbs 2G12, 670-D and 694/98D and not V3 MAbs – expression in rat brain also showed that surface expressed Env was recognized only by the conformation-dependent antibodies and not by anti-V3 antibodies [Altmeyer1999]
- 2G12: Hu-PBL-SCID mice were infected with HIV-1s JRCSF and SF162 to study the effect of NAbs on an established infection – no significant differences in the initial rate of decrease in viral load or the plateau levels of viral RNA between the b12 treated and control mice were seen – in most of the Ab treated mice b12 escape mutants were observed with varying patterns of mutations – a combination of b12, 2G12 and 2F5 protected 1/3 mice, and an isolate from one of the other two was resistant to neutralization by all three MAbs [Poignard1999]
- 2G12: Review of the neutralizing Ab response to HIV-1 [Parren1999]
- 2G12: Combinations of HIVIG, 2F5, 2G12 were administered in passive-transfer experiments 24 hours prior to challenge with pathogenic SHIV 89.6PD – 3/6 animals given HIVIG/2F5/2G12 were completely protected, the others had reduced viremia and normal CD4 counts – 1/3 monkeys given 2F5/2G12 showed transient infection, the other two had reduced viral load – all monkeys that received HIVIG, 2F5, or 2G12 alone became infected and developed high-level plasma viremia, although animals that got HIVIG or 2G12 had a less profound CD4 T cell decline [Mascola1999]
- 2G12: Because HIV-1 is most often transmitted across mucosal surfaces, the ability of passive transfer of infused HIVIG/2F5/2G12 to protect against mucosal exposure of macaques to pathogenic SHIV 89.6PD was studied – HIVIG/2F5/2G12 protected 4/5 animals against vaginal challenge, 2F5/2G12 combined protected 2/5 animals, and 2G12 alone protected 2/4 animals – in contrast, Mascola and co-workers had previously shown single MAbs could not protect against intervenous challenge – Ab treated animals that got infected through vaginal innoculation had low viral loads and only modest declines in CD4 counts – the infused Abs were detected in the nasal, vaginal, and oral mucosa [Mascola2000]
- 2G12: Combinations of HIVIG, 2F5, 2G12 were administered in passive-transfer experiments 24 hours prior to challenge with pathogenic SHIV 89.6PD – 3/6 animals given HIVIG/2F5/2G12 were completely protected, the others had reduced viremia and normal CD4 counts – 1/3 monkeys given 2F5/2G12 showed transient infection, the other two had reduced viral load – all monkeys that received HIVIG, 2F5, or 2G12 alone became infected and developed high-level plasma viremia, although animals that got HIVIG or 2G12 had a less profound CD4 T cell decline [Mascola1999]
- 2G12: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes [Binley1999]
- 2G12: A mini-review of observations of passive administration of IgG NAbs conferring protection against intervenous or vaginal SHIV challenge, that considers why IgG MAbs might protect against mucosal challenge [Robert-Guroff2000]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 2G12: A triple combination of 2F5, F105 and 2G12 effectively neutralized perinatal infection of macaque infants when challenged with SHIV-vpu+ – the mean plasma half-life was 14.0 +/- 7.9 days, the longest of the three Abs [Baba2000]
- 2G12: To determine the antigenicity of virus killed by thermal and chemical inactivation, retention of conformation-dependent neutralization epitopes was examined, and exposure of CD4BS epitopes was found to be enhanced (MAbs IgG1b12, 205-46-9, and 205-43-1) – binding to 2G12 and 447-52D epitopes was essentially unaltered – the 17b CD4i epitope was also exposed [Grovit-Ferbas2000]
- 2G12: Six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20-100 fold more efficient at neutralizing the sensitive form – 2G12 was an exception and could not neutralize MN in either form [Park2000]
- 2G12: SHIV-HXBc2 is a neutralization sensitive non-pathogenic virus, and several in vivo passages through monkey's yielded highly pathogenic SHIV KU-1 – HXBc2 and the KU-1 clone HXBc2P3.2 differ in 12 amino acids in gp160 – substitutions in both gp120 and gp41 reduced the ability of sCD4, IgG1b12, F105 and AG1121 to Env achieve saturation and full occupancy, and neutralize KU-1 – 17b and 2F5 also bound less efficiently to HXBc2P3.2, although 2G12 was able to bind both comparably [Si2001]
- 2G12: Neutralization synergy between anti-HIV NAbs b12, 2G12, 2F5, and 4E10 was studied – a classic fixed-ratio method was used, as well as a method where one Ab was fixed at a low neutralization titer and the other was varied – using primary isolates, a two-four fold enhancement of neutralization was observed with MAb pairs, and a ten-fold enhancement with a quadruple Ab combination – no synergy was observed with any MAb pair in the neutralization of TCLA strain HXB2 – there was no evidence for cooperativity of binding between b12 and 2G12 to envelope spikes expressed on the cell surface of TCLA or primary isolates [Zwick2001c]
- 2G12: Review of studies in macaques that have shown immune control of pathogenic SHIV viremia, improved clinical outcome, and protection, and the implications of the observations for HIV vaccines [Mascola2001]
- 2G12: SF162DeltaV2 is a virus that has a 30 amino acids deletion in the V2 loop that does not abrogate its infectivity but renders it highly susceptible to neutralization – when incorporated into a codon-optimized DNA vaccine with a CMV promoter and delivered by gene gun, SF162DeltaV2 gave higher neutralizing Ab titers against SF162 than did SF162 itself, and Abs that cross-neutralized non-homologous primary isolates were obtained only when SF162DeltaV2, but not intact SF162, was used as the immunogen – Control MAbs 2F5 and 2G12 could neutralize all of the following primary isolates: 91US056(R5), 92US714(R5), 92US660(R5), 92HT593(R5X4), and BZ167(R5X4), while after the first protein boost, the sera from two SF162DeltaV2 immunized macaques could neutralize 91US056(R5), 92US714(R5), 92US660(R5) and ADA(R5), but not 92HT593(R5X4) or 92US657(R5) – the pattern of cross-recognition shifted after the second boost [Barnett2001]
- 2G12: Moore and colleagues review structural aspects of gp120 and how they relate to antigenic domains, and review the data concerning the lack of a clear relationship between genetic subtype and serotype – an exception exists for human MAb 2G12, which does not recognize CRF01 envelopes because of an unusual additional disulfide bond in the V4 loop region that appears to be unique to the subtype E, CRF01 gp120 protein [Moore2001]
- 2G12: Structural aspects of the interaction of neutralizing Abs with HIV-1 Env are reviewed – Env essentially has three faces, one is largely inaccessible on the native trimer, and two that exposed but have low immunogenicity on primary viruses – neutralization is suggested to occur by inhibition of the interaction between gp120 and the target cell membrane receptors as a result of steric hindrance and it is noted that the attachment of approximately 70 IgG molecules per virion is required for neutralization, which is equivalent to about one IgG molecule per spike – the 2G12, 17b and b12 epitopes are discussed in detail – although it is potently neutralizing, 2G12 does not interfere with CD4 and coreceptor binding, and this Ab specificity is uncommon in sera from HIV-1-infected individuals [Poignard2001]
- 2G12: Neutralizing synergy between MAbs 1b12, 2G12 and 2F5 was studied using surface plasmon resonance to determine the binding kinetics for these three MAbs with respect to monomeric and oligomeric Env protein gp160 IIIB – the 2G12 epitope is highly accessible on both monomeric and oligomeric Envs, 1b12 is highly accessible on monomers but not oligomers, and 2F5 on neither form – binding of 2G12 exposes the 2F5 epitope on gp160 oligomers – 2G12-gp160 oligomer interactions were best fitted to a two state model, with the first complex having a high association constant and fast dissociation, that is stabilized by conformational changes induced by the binding of a second MAb [Zeder-Lutz2001]
- 2G12: A luciferase-reporter gene-expressing T-cell line was developed to facilitate neutralization and drug-sensitivity assays – luciferase and p24 antigen neutralization titer end points were found comparable using NAb from sera from HIV+ donors, and MAbs 2F5, 2G12 and IgG1b12 [Spenlehauer2001]

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- 2G12: A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6 – six gave significant neutralization at 2 to 10 ug/ml: 2F5, 50-69, IgG1b12, 447-52D, 2G12, and 670-D six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98-6, and 1281 – no synergy, only additive effects were seen for pairwise combinations of MAbs, and antagonism was noted between gp41 MAbs 50-69 and 98-6, as well as 98-6 and 2F5 [Verrier2001]
- 2G12: A combination of MAbs IgG1b12, 2F5, and 2G12 was given postnatally to four neonates macaques that were then challenged with highly pathogenic SHIV89.6P – one of the four infants remained uninfected after oral challenge, two infants had no or a delayed CD4(+) T-cell decline [Hofmann-Lehmann2001]
- 2G12: Twenty HIV clade C isolates from five different countries were susceptible to neutralization by anti-clade B MAbs in a synergistic quadruple combination of mAbs IgG1b12, 2G12, 2F5, and 4E10 [Xu2001]
- 2G12: Chloroquine reduces the HIV-1-infectivity of H9 IIIB cells, apparently through altering the conformation of envelope – there is a reduction of reactivity of 2G12 to its epitope in chloroquine treated cultures [Savarino2001]
- 2G12: A phase I trial in seven HIV+ individuals was conducted with MAbs 2F5 and 2G12—no clinical or laboratory abnormalities were observed throughout the study—eight infusions were administered over a 4-week period (total dose 14 g)—the elimination half-life ($t\_1/2$) was calculated to be 7.94 (range, 3.46–8.31) days for 2F5 and 16.48 (range, 12.84–24.85) days for 2G12 [Armbruster2002].
- 2G12: The fusion process was slowed by using a suboptimal temperature (31.5 C) to re-evaluate the potential of Abs targeting fusion intermediates to block HIV entry – preincubation of E/T cells at 31.5 C enabled polyclonal anti-N-HR Ab and anti-six-helix bundle Abs to inhibit fusion, indicating six-helix bundles form prior to fusion – the preincubation 31.5 C step did not alter the inhibitory activity of neutralizing Abs anti-gp41 2F5, or anti-gp120 2G12, IG1b12, 48d, and 17b [Golding2002b]
- 2G12: The 2G12 epitope is composed of carbohydrates involving high-mannose and hybrid glycans of residues 295, 332, and 392, with peripheral glycans from 386 and 448 contributing on either flank, and with little direct gp120 protein surface involvement – these mannose residues are proximal to each other near the chemokine receptor binding surface [Sanders2002]
- 2G12: Alanine scanning mutagenesis used in conjunction with competition and replacement studies of N-linked carbohydrates and sugars suggest that the 2G12 epitope is formed from mannose residues contributed by the glycans attached to N295 and N332, with the other N-linked carbohydrates in positions N339, N386, and N392 playing a role in maintaining conformation relevant to 2G12 binding – N295A and N332A mutants showed essentially unchanged anti-CD4BS NAb b12 binding affinities, while N339A, N386A and N392A mutants displayed significantly lowered b12 affinity, presumably due to conformational changes [Scanlan2002]
- 2G12: Ab binding characteristics of SOS gp140 were tested using SPR and RIPA – SOS gp140 is gp120-gp41 bound by a disulfide bond – NAbs 2G12, 2F5, IgG1b12, CD4 inducible 17b, and 19b bound to SOS gp140 better than uncleaved gp140 (gp140unc) and gp120 – non-neutralizing MAbs 2.2B (binds to gp41 in gp140unc) and 23A (binds gp120) did not bind SOS gp140 – 2G12 complexes with SOS gp140 or with gp120 had a very unusual linear structure [Schulke2002]
- 2G12: Uncleaved soluble gp140 (YU2 strain, R5 primary isolate) can be stabilized in an oligomer by fusion with a C-term trimeric GCN4 motif or using a T4 trimeric motif derived from T4 bacteriophage fibritin – stabilized oligomer gp140 delta683(-FT) showed strong preferential recognition by NAbs IgG1b12 and 2G12 relative to the gp120 monomer, in contrast to poorly neutralizing MAbs F105, F91, 17b, 48d, and 39F which showed reduced levels of binding, and MAbs C11, A32, and 30D which did not bind the stabilized oligomer [Yang2002]
- 2G12: Passive immunization of neonate macaques with a combination of F105+2G12+2F5 conferred complete protection against oral challenge with SHIV-vpu+ or – the combination b12+2G12+2F5 conferred partial protection against SHIV89.6 – such combinations may be useful for prophylaxis at birth and against milk born transmission – the synergistic combination of IgG1b12, 2G12, 2F5, and 4E10 neutralized a collection of HIV clade C primary isolates [Xu2002]
- 2G12: A modified gp140 (gp140deltaCFI), with C-term mutations intended to mimic a fusion intermediate and stabilize trimer formation, retained antigenic conformational determinants as defined by binding to CD4 and to MAbs 2F5, 2G12, F105, and b12, and enhanced humoral immunity without diminishing the CTL response in mice injected with a DNA vaccine [Chakrabarti2002]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 2G12: A combination of MAbs 2F5 and 2G12 given in multiple infusions was found to be safe and well tolerated even in high doses in a phase I study of seven HIV-1 infected healthy volunteers – the median elimination half-life was 7.94 days for 2F5, and 16.48 for 2G12 – no anti-2F5 or anti-2G12 IgM or IgG responses were detected – although there was some transient increases, overall plasma viral RNA levels decreased in 6/7 volunteers, by a median of 0.62 log_10 [Armbruster2002]
- 2G12: Truncation of the gp41 cytoplasmic domain of X4, R5, and X4R5 viruses forces a conformation that more closely resembles the CD4 bound state of the external Envelope, enhancing binding of CD4i MAbs 17b and 48d and of CD4BS MAbs F105, b12, and in most cases of glycosylation site dependent MAb 2G12 and the anti-gp41 MAb 246D – in contrast, binding of the anti-V2 MAb 697D and the anti-V3 MAb 694/98D were not affected – viruses bearing the truncation were more sensitive to neutralization by MAbs 48d, b12, and 2G12 – the anti-C5 MAb 1331A was used to track levels of cell surface expression of the mutated proteins [Edwards2002]
- 2G12: HIV-1 gp160deltaCT (cytoplasmic tail-deleted) proteoliposomes (PLs) containing native, trimeric envelope glycoproteins from R5 strains YU2 and JRFL, and X4 strain HXBc2, were made in a physiologic membrane setting as candidate immunogens for HIV vaccines – 2F5 bound to gp160deltaCT with a reconstituted membrane ten-fold better than the same protein on beads, while such an affinity difference was not seen with F105 and 2G12 – anti-CD4BS MAbs IgG1b12 and F105, A32 (C1-C4), C11 (C1-C5), and 39F (V3) MAbs bound gp160deltaCT PLs indistinguishably from gp160deltaCT expressed on the cell surface [Grundner2002]
- 2G12: Rhesus macaques were better protected from vaginal challenge with SHIV89.6D (MAb 2G12, 2/4; MAbs 2F5/2G12, 2/5; and HIVIG/2F5/2G12, 4/5 infected) than from intravenous challenge (MAb 2G12, 0/3; MAbs 2F5/2G12, 1/3; and HIVIG/2F5/2G12, 3/6 infected)– the animals that were infected by vaginal challenge after Ab infusion had low or undetectable viral RNA levels and modest CD4 T-cell decline [Mascola2002]
- 2G12: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain [Zhang2002]
- 2G12: Review of NAbs that notes 2G12 alone or in combination with other MAbs can protect some macaques against SHIV infection, that it has strong ADCC activity, and that it is safe and well tolerated in humans [Ferrantelli2002]
- 2G12: Review of NAbs that discusses mechanisms of neutralization, passive transfer of NAbs and protection in animal studies, and vaccine strategies [Liu2002]
- 2G12: Alanine scanning mutagenesis was used to compare substitutions that affected anti-CD4BS NAb b12 – rec gp120s were engineered to contain combinations of Alanine substitutions that enhanced b12 binding, and while binding of b12 to these gp120 monomers was generally maintained or increased, binding by five non-neutralizing anti-CD4bs MAbs (b3, b6, F105, 15e, and F91) was reduced or completely abolished – 2G12 binding was largely unperturbed, indicating these proteins were not grossly misfolded [Pantophlet2003]
- 2G12: CD4BS MAbs b12 (neutralizing) and 205-42-15, 204-43-1, 205-46-9 (nonneutralizing) all cross-competed for binding to monomeric gp120, indicating the topological proximity of their epitopes, however, the nonneutralizing CD4BS MAbs did not interfere with the neutralization activity of MAb b12 – 2G12 was used to normalize and as a control in these experiments [Herrera2003]
- 2G12: UK Medical Research council AIDS reagent: ARP3030
- 2G12: NIH AIDS Research and Reference Reagent Program: 1476

1046	1367	Env	gp41		HIV-1 infection		human (IgG1λ)

Ab type cluster I **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Nyambi1998, Gorny2000b, Gorny2000a, Nyambi2000

- 1367: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – anti-gp41 Abs 98-6, 1367 and 1342 were not able to bind detectably with any of the viruses from any clade [Nyambi1998]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 1367: A cluster I epitope that binds to rgp41 567-647, recognizes a peptide N51-C43 complex trimer of heterodimers that approximates the core of the fusogenic form of gp41 – this MAb doesn't react with either of the peptides N51 or C43 individually – MAbs 50-69 and 1367 had similar properties [Gorny2000b]
- 1367: Binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, but gp41 MAb 50-69 bound with a 5 fold preference for the oligomer, while other gp41 MAbs (1367, 98-6, 167-D, 1281, 1342, and 1379) did not show a preference [Gorny2000a]
- 1367: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 5 cluster I anti-gp41 MAbs which showed good cross clade reactivity – 1367 weakly bound to the majority of isolates – no neutralizing activity was observed when tested with 5 isolates, but 1367 did not bind well to these isolates [Nyambi2000]

1047 126-6 (SZ-126.6) | Env | gp41 (HXB2) | | no | HIV-1 infection | human (IgG2κ)

Ab type cluster II **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU Med Center, NY, NY

References Robinson1990b, Robinson1991, Xu1991, Eddleston1993, Chen1995, Binley1996, Earl1997, Hioe1997b, Gorny2000b, Nyambi2000

- 126-6: No enhancing activity for HIV-1 IIIB [Robinson1990b]
- 126-6: No enhancing or neutralizing activity [Robinson1991]
- 126-6: Specific for a conformational epitope [Xu1991]
- 126-6: Called SZ-126.6 [Eddleston1993]
- 126-6: One of several anti-gp41 MAbs that bind to a gp41-maltose binding fusion protein designed to study the leucine zipper domain of gp41, showing that the construct has retained aspects of normal gp41 conformation [Chen1995]
- 126-6: Discontinuous epitope recognizing residues between 649-668 – designated cluster II – Fabs D5, D11, G1, T3, M12, M15, S6, S8, S9, S10 block binding [Binley1996]
- 126-6: This cluster II MAb binds to a conformational epitope in the region 644-663 – like most cluster II MAbs (126-6, 167-D, 1281, 1342, and 1379 all reacted similarly) it binds to a peptide N51-C43 complex trimer of heterodimers that approximates the core of the fusogenic form of gp41, but not to C43 nor to N51 alone – MAb 126-6 was biotinylated and used as a probe to determine that anti-gp41 MAb 50-69 bound the fusogenic form of the protein in liquid phase [Gorny2000b]
- 126-6: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 cluster II anti-gp41 MAbs – of these 2F5, 167-D, 126-6, and 1281 bound across clades, but usually weakly, while 98-6 and 1342 had poor cross reactivity – Clade D isolates bound most consistently to cluster II MAbs [Nyambi2000]
- 126-6: NIH AIDS Research and Reference Reagent Program: 1243

1048 1342 | Env | gp41 | | no | HIV-1 infection | human (IgG1λ)

Ab type cluster II **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)

References Nyambi1998, Gorny2000b, Gorny2000a, Nyambi2000

- 1342: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – anti-gp41 Abs 98-6, 1367 and 1342 were not able to bind detectably with any of the viruses from any clade [Nyambi1998]
- 1342: This cluster II MAb is a conformational epitope that binds in the region 644-663 – like most cluster II MAbs (126-6, 167-D, 1281, 1342, and 1379 all reacted similarly) it binds to a peptide N51-C43 complex trimer of heterodimers that approximates the core of the fusogenic form of gp41, but not to C43 nor to N51 alone [Gorny2000b]
- 1342: Binds within the region gp41 647-682 – binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, but gp41 MAb 50-69 bound with a 5 fold preference for the oligomer, while other gp41 MAbs (1367, 98-6, 167-D, 1281, 1342, and 1379) did not show a preference [Gorny2000a]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 1342: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 cluster II anti-gp41 MAbs – of these 2F5, 167-D, 126-6, and 1281 bound across clades, but usually weakly, while 98-6 and 1342 had poor cross reactivity – Clade D isolates bound most consistently to cluster II MAbs – no neutralizing activity was observed when tested with 5 isolates, but 1342 did not bind to these isolates [Nyambi2000]					
1049	1379	Env	gp41			HIV-1 infection	human (IgG1λ)
		Ab type cluster II **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center) **References** Gorny2000b, Gorny2000a • 1379: This cluster II MAb binds to a conformational epitope in the region 644-663 – like most cluster II MAbs (126-6, 167-D, 1281, 1342, and 1379 all reacted similarly) it binds to a peptide N51-C43 complex trimer of heterodimers that approximates the core of the fusogenic form of gp41, but not to C43 nor to N51 alone [Gorny2000b] • 1379: Binds within the region gp41 647-682 – binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, but gp41 MAb 50-69 bound with a 5 fold preference for the oligomer, while other gp41 MAbs (1367, 98-6, 167-D, 1281, 1342, and 1379) did not show a preference [Gorny2000a]					
1050	Fab D11	Env	gp41 (LAI)		no	HIV-1 infection	human (IgG1κ)
		Ab type cluster II **References** Binley1996 • Fab D11: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced [Binley1996]					
1051	Fab D5	Env	gp41 (LAI)		no	HIV-1 infection	human (IgG1κ)
		Ab type cluster II **References** Binley1996 • Fab D5: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced [Binley1996]					
1052	Fab G1	Env	gp41 (LAI)		no	HIV-1 infection	human (IgG1κ)
		Ab type cluster II **References** Binley1996 • Fab G1: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced [Binley1996]					
1053	Fab M10	Env	gp41 (LAI)		no	HIV-1 infection	human (IgG1κ)
		Ab type cluster II **References** Binley1996, Parren1997c • Fab M10: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced [Binley1996] • Fab M10: Does not bind to MN native oligomer, but does bind to both LAI and MN rgp120 and rgp140 [Parren1997c]					
1054	Fab M12	Env	gp41 (LAI)		no	HIV-1 infection	human (IgG1κ)
		Ab type cluster II **References** Binley1996 • Fab M12: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced [Binley1996]					
1055	Fab M15	Env	gp41 (LAI)		no	HIV-1 infection	human (IgG1κ)
		Ab type cluster II **References** Binley1996 • Fab M15: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced [Binley1996]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
1056	Fab S10	Env	gp41 (LAI)		no	HIV-1 infection	human (IgG1κ)
		Ab type cluster II					
		References Binley1996					
		• Fab S10: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced [Binley1996]					
1057	Fab S6	Env	gp41 (LAI)		no	HIV-1 infection	human (IgG1κ)
		Ab type cluster II					
		References Binley1996					
		• Fab S6: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced [Binley1996]					
1058	Fab S8	Env	gp41 (LAI)		no	HIV-1 infection	human (IgG1κ)
		Ab type cluster II					
		References Binley1996					
		• Fab S8: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced [Binley1996]					
1059	Fab S9	Env	gp41 (LAI)		no	HIV-1 infection	human (IgG1κ)
		Ab type cluster II					
		References Binley1996					
		• Fab S9: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced [Binley1996]					
1060	Fab T3	Env	gp41 (LAI)		no	HIV-1 infection	human (IgG1κ)
		Ab type cluster II					
		References Binley1996					
		• Fab T3: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced [Binley1996]					
1061	Md-1 (MD-1)	Env	gp41		no		human (IgG1λ)
		Ab type cluster II **Donor** R. A. Myers State of Maryland Dept. of Health					
		References Myers1993, Chen1995, Binley1996					
		• Md-1: Called MD-1 – discontinuous epitope that binds in the N-terminal region – reacts exclusively with oligomer [Myers1993]					
		• Md-1: Called MD-1 – one of several anti-gp41 MAbs that bind to a gp41-maltose binding fusion protein designed to study the leucine zipper domain of gp41, showing that the construct has retained aspects of normal gp41 conformation [Chen1995]					
		• Md-1: Discontinuous epitope recognizing residues between 563-672, does not recognize cluster I disulfide bridge region – reacts almost exclusively with trimers and tetramers on WB – designated cluster II – Fabs D5, D11, G1, T3, M12, M15, S6, S8, S9, S10 block binding [Binley1996]					
		• Md-1: NIH AIDS Research and Reference Reagent Program: 1223					
1062	1281 (1281-D)	Env	gp41			HIV-1 infection	human (IgG1λ)
		Ab type cluster II, six-helix bundle **Donor** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)					
		References Hioe1997b, Gorny2000b, Gorny2000a, Verrier2001, Golding2002b					
		• 1281: Called 1281-D: Four primary isolates showed distinct patterns of sensitivity to neutralization by polyclonal sera or plasma and MAbs – BZ167 was the only isolate inhibited by all polyclonal sera and plasma tested, and was also neutralized by 8/17 MAbs, in particular anti-V3 loop (419-D, 447-52D, 782-D, and 838-D), anti-CD4bd (559/64-D, 654-D and 830-D and a cluster II of gp41 directed MAb (98-6) – isolates 92HT593 and 91US056 were neutralized by V3 loop (419-D, and 447-52D)and cluster II gp41 (98-6) MAbs at higher concentrations – US4 was neutralized by some of the polyclonal sera/plasma tested and not at all by MAbs individually or by a cocktail of ten MAbs consisting of 419-D, 447-52D, 782-D, 838-D, 559/64-D, 654-D, 450-D, 670-D, 1281-D and 98-6 [Hioe1997b]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 1281: This cluster II MAb binds to a conformational epitope in the region 644-663 – like most cluster II MAbs (126-6, 167-D, 1281, 1342, and 1379 all reacted similarly) it binds to a peptide N51-C43 complex trimer of heterodimers that approximates the core of the fusogenic form of gp41, but not to C43 nor to N51 alone [Gorny2000b] • 1281: Binds within the region gp41 647-682 – binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, but gp41 MAb 50-69 bound with a 5 fold preference for the oligomer, while other gp41 MAbs (1367, 98-6, 167-D, 1281, 1342, and 1379) did not show a preference [Gorny2000a] • 1281: A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6 – six gave significant neutralization at 2 to 10 ug/ml: 2F5, 50-69, IgG1b12, 447-52D, 2G12, and 670-D six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98-6, and 1281 – no synergy, only additive effects were seen for pairwise combinations of MAbs, and antagonism was noted between gp41 MAbs 50-69 and 98-6, as well as 98-6 and 2F5 [Verrier2001] • 1281: The fusion process was slowed by using a suboptimal temperature (31.5 C) to re-evaluate the potential of Abs targeting fusion intermediates to block HIV entry – preincubation of E/T cells at 31.5 C enabled polyclonal anti-N-HR Ab and anti-six-helix bundle Abs to inhibit fusion, indicating six-helix bundles form prior to fusion – 98-6 binds to a C-HR hairpin epitope and blocks fusion when added to a 2 hour E/T preincubation at 31.5 C, but if added after 1 hour, doesn't inhibit – this is in contrast to six-helix bundle Abs 167-D and 1281 that inhibit more efficiently when added after one hour of incubation [Golding2002b]				
1063	Fab A9	Env	gp41 (LAI)		no	HIV-1 infection	human (IgG1κ)
		Ab type cluster III **References** Binley1996 • Fab A9: Binds to cluster III region – competes with MAb Md-1, but not MAbs 126-6 and D50 – conformation sensitive – variable regions sequenced [Binley1996]					
1064	Fab G15	Env	gp41 (LAI)		no	HIV-1 infection	human (IgG1κ)
		Ab type cluster III **References** Binley1996 • Fab G15: Binds to cluster III region – competes with MAb Md-1, but not MAbs 126-6 and D50 – conformation sensitive – variable regions sequenced [Binley1996]					
1065	Fab G5	Env	gp41 (LAI)		no	HIV-1 infection	human (IgG1κ)
		Ab type cluster III **References** Binley1996 • Fab G5: Binds to cluster III region – competes with MAb Md-1, but not MAbs 126-6 and D50 – conformation sensitive – variable regions sequenced [Binley1996]					
1066	Fab L1	Env	gp41 (LAI)		no	HIV-1 infection	human (IgG1κ)
		Ab type cluster III **References** Binley1996 • Fab L1: Binds to cluster III region – competes with MAb Md-1, but not MAbs 126-6 and D50 – conformation sensitive – variable regions sequenced [Binley1996]					
1067	Fab L11	Env	gp41 (LAI)		no	HIV-1 infection	human (IgG1κ)
		Ab type cluster III **References** Binley1996					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• Fab L11: Binds to cluster III region – competes with MAb Md-1, but not MAbs 126-6 and D50 – conformation sensitive – variable regions sequenced [Binley1996]					
1068	Fab L2	Env	gp41 (LAI)		no	HIV-1 infection	human (IgG1κ)
		Ab type cluster III **Donor** P. Perrin and D. Burton (Scripps Research Institute, La Jolla, California **References** Binley1996, Earl1997 • Fab L2: Binds to cluster III region – competes with MAb Md-1, but not MAbs 126-6 and D50 – conformation sensitive – variable regions sequenced [Binley1996]					
1069	Chessie 8	Env	gp41				murine (IgG)
		Ab type cytoplasmic domain **Donor** G. Lewis **References** Lewis1991, Poumbourios1995, Rovinski1995, Smith-Franklin2002 • Chessie 8: Used to precipitate gp160 in immunoblots in a study examining the feasibility of using unprocessed gp160 glycoprotein as an immunogen [Rovinski1995] • Chessie 8: This Ab was used in an in vitro study demonstrating that HIV-1 antibody and Fcgamma receptors can trap virus on the surface of follicular dendritic cells (FDC)'s and extend the period of infectivity – blocking the FDC-Fcgamma receptor killing the FDC cell reduced their ability to maintain infectivity, and FDC cells seemed to stabilize viral particles and decrease gp120 shedding [Smith-Franklin2002]					
1070	8F101	Env	gp120			Vaccine	murine (IgG)
		Vaccine *Vector/Type:* sCD4-gp120 complex *Strain:* HXB2 *HIV component:* gp120 **Ab type** gp120-CD4 complex **References** DeVico1995 • 8F101: MAbs specifically reactive to crosslinked gp120 and CD4 were derived (8F101, 8F102) – conformation dependent – competition studies indicate the epitope is immunogenic in infected humans [DeVico1995]					
1071	8F102	Env	gp120			Vaccine	murine (IgG)
		Vaccine *Vector/Type:* sCD4-gp120 complex *Strain:* HXB2 *HIV component:* gp120 **Ab type** gp120-CD4 complex **References** DeVico1995 • 8F102: MAbs specifically reactive to crosslinked gp120 and CD4 were derived (8F101, 8F102) – conformation dependent – competition studies indicate the epitope is immunogenic in infected humans [DeVico1995]					
1072	CG-10 (CG10)	Env	gp120 (IIIB)		L	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* sCD4-gp120 complex *Strain:* IIIB *HIV component:* gp120 **Ab type** gp120-CD4 complex **Donor** Jonathan Gershoni, Tel Aviv University, Isreal **References** Gershoni1993, Wu1996, Lee1997, Rizzuto1998, Sullivan1998b, Oscherwitz1999a • CG-10: Reacts exclusively with sCD4-gp120 complex, not with sCD4 or gp120 alone [Gershoni1993] • CG-10: Called CG10 – MIP-1alpha binding to CCR-5 expressing cells can be inhibited by gp120-sCD4, and MAb CG10 does not block this inhibition [Wu1996] • CG-10: Called CG10 – Promotes envelope mediated cell fusion between CD4+ cells and cells infected with either T-cell and macrophage tropic viruses – infection of HeLa CD4+ (MAGI) cells by HIV-1 LAI, ELI1, and ELI2 strains was increased two-to four-fold in the presence of CG10 [Lee1997] • CG-10: Called CG10 – disrupts gp120-CCR5 interaction and competes with MAb 17b –binds near the conserved bridging sheet of gp120 – mutations in positions K/D 121, T/D 123, K/D 207, K/D 421, Q/L 422, Y/S 435, M/A 434, K/A 432 and I/S 423 result in a 70% reduction in CG10 binding [Rizzuto1998]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• CG-10: Called CG10 – CD4BS MAb 15e competes with CG-10 binding, probably due to the disruption of CD4-gp120 by 15e – CD4i MAbs 17b and 48d compete and the binding sites may overlap – MAb A32 enhances binding of 17b, 48d and CG10 – MAbs C11, 2G12 and 212A do not affect CG10 binding – CG-10 can bind gp120 with V1/V2 and V3 deleted – HXBc2 mutations Delta 119-205, 314 G/W, 432 K/A, 183,184 PI/SG decrease CG-10 recognition, HXBc2 mutations Delta 298-327 (V3), 384 Y/E, 298 R/G, 435 Y/S enhance recognition – the CD4 contribution to the CG10 epitope maps to the CD4 CDR2-like loop – CG10 can neutralize HIV-1 in the presence of sCD4 even though it does not do so in the context of cell surface CD4 binding to gp120 [Sullivan1998b]				
1073	CG-25	Env	gp120		L	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* sCD4-gp120 complex *HIV component:* gp120 **Ab type** gp120-CD4 complex **References** Gershoni1993 • CG-25: Reacts preferentially with sCD4-gp120, also with sCD4, not with gp120 [Gershoni1993]					
1074	CG-4 (CG4)	Env	gp120		no	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* sCD4-gp120 complex *HIV component:* gp120 **Ab type** gp120-CD4 complex **Donor** Jonathan Gershoni, Tel Aviv University, Isreal **References** Gershoni1993 • CG-4: Reacts with gp120 and sCD4-gp120 complex, not with sCD4 [Gershoni1993]					
1075	CG-76	Env	gp120		L	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* sCD4-gp120 complex *HIV component:* gp120 **Ab type** gp120-CD4 complex **References** Gershoni1993 • CG-76: Reacts equally well with sCD4-gp120 and sCD4, but not with purified gp120 [Gershoni1993]					
1076	CG-9	Env	gp120		L	Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* sCD4-gp120 complex *HIV component:* gp120 **Ab type** gp120-CD4 complex **References** Gershoni1993 • CG-9: Reacts preferentially with sCD4-gp120, also with sCD4, not with gp120 [Gershoni1993]					
1077	105-518	Env	gp41 (608–637 HAM112, O group)			Vaccine	murine (IgG1 κ)
		Vaccine *Vector/Type:* recombinant protein *Strain:* HAM112 (group O) *HIV component:* gp160 **Ab type** immunodominant region **References** Scheffel1999 • 101-518: Overlapping peptides based on group O HAM112 Env were tested for MAb reactivity [Scheffel1999]					
1078	31A1	Env	gp41		no	in vitro stimulation	human (IgMκ/λ)
		Ab type p24+gp41 **References** Pollock1989 • 31A1: Denatured virus was used for in vitro stimulation to generate Abs – Reacts with both p24 and gp41 [Pollock1989]					
1079	39A64	Env	gp41		no	in vitro stimulation	human (IgMκ/λ)
		Ab type p24+gp41					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Pollock1989					
		• 39A64: Denatured virus was used for in vitro stimulation to generate Abs – Reacts with both p24 and gp41 [Pollock1989]					
1080	39B86	Env	gp41		no	in vitro stimulation	human (IgMκ/λ)
		Ab type p24+gp41					
		References Pollock1989					
		• 39B86: Denatured virus was used for in vitro stimulation to generate Abs – Reacts with both p24 and gp41 [Pollock1989]					
1081	9303	Env	gp41		no		murine
		Ab type p24+gp41 **Donor** Du Pont					
		References McDougal1996					
1082	NC-1	Env	gp41 (IIIB)			Vaccine	murine (IgG2a)
		Vaccine *Vector/Type:* peptide *Strain:* IIIB *HIV component:* a peptide that folds into a six helix bundle like gp41					
		Ab type six helix bundle **Donor** S. Jiang, New York Blood Center, NY, NY					
		References Jiang1998, Yang2000, Yang2002					
		• NC-1: Ab elicited in response to immunization with N36(L6)C34, a peptide that folds into a six helix bundle like gp41 – NC-1 binds to the surface of HIV-1 infected cells only in the presence of sCD4, recognizing the fusogenic core structure – binding affinity was decreased by point mutations that disrupt core formation and abolish membrane fusion activity, (I573P and I573A) – NC-1 can recognize discontinuous epitopes from B clade isolate SC, but not E clade strain N243, O group strain GAB, or HIV-2 ROD [Jiang1998]					
		• NC-1: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) – approximately 16% of the gp140(-GNC4) stabilized trimer recognized by pooled sera was precipitated by NC-1, indicating that at a fraction assumes a fusogenic gp41 six-helix bundle conformation – gp140(-) monomers were not able to bind to the NC-1, nor was gp130(-/GCN4) glycoprotein, consistent with the expectation that the absence of C34 helices would preclude formation of the six-helix bundle [Yang2000]					
		• NC-1: Uncleaved soluble gp140 can be stabilized in an oligomer by fusion with a C-term trimeric GCN4 motif (gp140delta683(-/GCN4)) or using a T4 trimeric motif derived from T4 bacteriophage fibritin (gp140delta683(-/FT)) – NC-1 binds to 15% of the GCN4 motif trimers, but this was significantly reduced for the T4 fibritin stabilized structures, indicating little is in the six-helix bundle, fusogenic conformation [Yang2002]					

IV-C-15 Nef Antibodies

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
1083	4H4	Nef (1–33)	Nef (1–33 IIIB)	MGGKWSKSSVVGWPTVRERMRRAPT-VRERMRRAEPAADGVGAA		Vaccine	human (IgG1)
		Vaccine *Vector/Type:* recombinant protein *Strain:* IIIB *HIV component:* Nef **References** Otake1994 • 4H4: This MAb, elicited by vaccination with a Nef fusion protein, could not detect Nef protein on the cell surface – C-term anti-Nef Abs could [Otake1994]					
1084	polyclonal	Nef (9–24)	Nef (9–24)	SVIGWLTVRERMRRAE	no	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* DNA *Strain:* BRU *HIV component:* Nef **References** Tahtinen2001 • BALB/c mice were immunized with a pBN-vector expressing HIV-1 nef, rev, or tat genes – DNA loaded onto gold microparticles was delivered using a gene gun, and DNA dissolved in saline was given intradermally or intramuscularly – Nef gene gun immunized mice showed the strongest and most long-lasting (6 months) Ab, CTL and proliferative responses – the highest IgG1/IgG2a ratio was observed in the gene gun immunized mice – three Ab binding sites were found in Nef using peptide mapping, although some sera reacted only to complete Nef – Rev- or-Tat immunized mice did not generate an Ab response [Tahtinen2001]					
1085	13/042	Nef (11–20)	Nef (11–24 BH10)	VGWPTVRERM		Vaccine	murine
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Nef **References** Schneider1991 • 13/042: Epitope mapped by overlapping decapeptides – core: TVRERM [Schneider1991]					
1086	13/035	Nef (15–24)	Nef (11–24 BH10)	TVRERMRRAE		Vaccine	murine
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Nef **References** Schneider1991 • 13/035: Epitope mapped by overlapping decapeptides – core: TVRERM [Schneider1991]					
1087	AM5C6	Nef (28–43 + 78–92)	Nef (28–43 BH10)	DGVGAASRDLEKHGAI+KAAVDLSH-FLK		Vaccine	murine
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Nef **References** Schneider1991, Maksiutov2002 • AM5C6: Epitope mapped by overlapping decapeptides – core: SRDL – also reacts with Nef(78-92) [Schneider1991] • AM5C6: This epitope is similar to a fragment of the human protein vascular endothelial growth factor C, AEPDAGEATAYASKDLE [Maksiutov2002]					
1088	AM5C6	Nef (28–43 + 78–92)	Nef (28–43 BH10)	DGVGAASRDLEKHGAI+KAAVDLSH-FLK		Vaccine	murine
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Nef **References** Schneider1991, Maksiutov2002 • AM5C6: Epitope mapped by overlapping decapeptides – core: KAAVDL – also reacts with Nef(28-43) [Schneider1991] • AM5C6: This epitope is similar to a fragment of the human protein vascular endothelial growth factor C, AEPDAGEATAYASKDLE [Maksiutov2002]					
1089	25/03	Nef (30–43)	Nef (30–43 BH10)	VGAASRDLEKHGAI		Vaccine	murine
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Nef **References** Schneider1991, Maksiutov2002					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 25/03: Epitope mapped by overlapping decapeptides – core: ASRDLEK [Schneider1991] • 25/03: This epitope is similar to a fragment of the human protein vascular endothelial growth factor C, AEPDAGEATAYASKDLE [Maksiutov2002]					
1090	26/76	Nef (30–43)	Nef (30–43 BH10)	VGAASRDLEKHGAI		Vaccine	murine
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Nef **References** Schneider1991, Maksiutov2002 • 26/76: Epitope mapped by overlapping decapeptides – core: SRDLEK [Schneider1991] • 26/76: This epitope is similar to a fragment of the human protein vascular endothelial growth factor C, AEPDAGEATAYASKDLE [Maksiutov2002]					
1091	3F2	Nef (31–40)	Nef (31–40 BRU)	GAASRDLEKH		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *Strain:* BRU *HIV component:* Nef **References** Ovod1992, Saito1994, Ranki1995, Maksiutov2002 • 3F2: Reacted with Nef from different HIV-1 strains (BRU, IIIB, RF, MN) [Ovod1992] • 3F2: Faintly cross-reactive with astrocytes of uninfected control samples [Ranki1995] • 3F2: This epitope is similar to a fragment of the human protein vascular endothelial growth factor C, AEPDAGEATAYASKDLE [Maksiutov2002] • 3F2: UK Medical Research Council AIDS reagent: EVA3067.1					
1092	3D12	Nef (31–50)	Nef (31–50 BRU)	GAASRDLEKHGAITSSNTAA		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *Strain:* BRU *HIV component:* Nef **References** Ovod1992, Saito1994, Ranki1995, Maksiutov2002 • 3D12: There is an anti-RT MAb that also has this name (see [Chiba1997] • 3D12: Reacted with Nef from different HIV-1 strains (BRU, IIIB, RF, MN) [Ovod1992] • 3D12: Over-expression of Nef in astrocytes from postmortem pediatric CNS tissues [Saito1994] • 3D12: One of four antibodies used in combination to show HIV Nef protein expressed in astrocytes from 7/14 brain samples from HIV+ individuals – Nef expression associated with dementia [Ranki1995] • 3D12: This epitope is similar to a fragment of the human protein vascular endothelial growth factor C, AEPDAGEATAYASKDLE [Maksiutov2002] • 3D12: UK Medical Research Council AIDS reagent: EVA3067.2					
1093	polyclonal	Nef (33–65)	Nef (32–64 LAI, BRU)	ASRDLEKHGAITSSNTAATNAACAW–LEAQEEEE		HIV-1 infection, Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* PLG, recombinant protein *Strain:* LAI, BRU *HIV component:* Nef *Adjuvant:* PLG, complete Freund's adjuvant (CFA) **References** Moureau2002, Maksiutov2002 • Nef encapsulated in poly(DL-lactide-co-glycolide) (PLG) had a more prolonged Ab response than Nef in PBS or in Freund's adjuvant (CFA), still strong after 7 months – the response was predominantly IgG1, a Th2 immune response – three linear epitopes, Nef 32-64, 118-167, and 185-205, were frequently recognized by the sera of mice immunized with NefPLG or Nef-CFA, but not after immunization with Nef in PBS, which seemed to preferentially stimulate an Ab response to conformational epitopes [Moureau2002] • This epitope is similar to a fragment of the human protein vascular endothelial growth factor C, AEPDAGEATAYASKDLE [Maksiutov2002]					
1094	polyclonal	Nef (49–64)	Nef (49–64)	AATNAACAWLEAQEEE	no	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* DNA *Strain:* BRU *HIV component:* Nef **References** Tahtinen2001					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• BALB/c mice were immunized with a pBN-vector expressing HIV-1 nef, rev, or tat genes – DNA loaded onto gold microparticles was delivered using a gene gun, and DNA dissolved in saline was given intradermally or intramuscularly – Nef gene gun immunized mice showed the strongest and most long-lasting (6 months) Ab, CTL and proliferative responses – the highest IgG1/IgG2a ratio was observed in the gene gun immunized mice – three Ab binding sites were found in Nef using peptide mapping, although some sera reacted only to complete Nef – Rev- or-Tat immunized mice did not generate an Ab response [Tahtinen2001]					
1095	3G12	Nef (51–71)	Nef (51–71 BRU)	TNAACAWLEAQEEEEVGFPVT		Vaccine	murine (IgG2a)
		Vaccine *Vector/Type:* recombinant protein *Strain:* BRU *HIV component:* Nef **References** Ovod1992 • 3G12: Reacted with Nef from different HIV-1 strains (BRU, IIIB, RF, MN) [Ovod1992]					
1096	13/058	Nef (60–73)	Nef (60–73 BH10)	AQEEEEVGFPVTPQ		Vaccine	murine
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Nef **References** Schneider1991 • 13/058: Epitope mapped by overlapping decapeptides – core: EEVGFP [Schneider1991]					
1097	26/028	Nef (60–73)	Nef (60–73 BH10)	AQEEEEVGFPVTPQ		Vaccine	murine
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Nef **References** Schneider1991 • 26/028: Epitope mapped by overlapping decapeptides – core: EEVGFPV [Schneider1991]					
1098	2E3	Nef (61–80)	Nef (61–80 BRU)	QEEEEVGFPVTPQVPLRPMT		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *Strain:* BRU *HIV component:* Nef **References** Ovod1992, Nilsen1996 • 2E3: There are two MAbs with the name 2E3 – the other one binds to integrase [Nilsen1996] • 2E3: Two isomorphic forms of Nef were identified, 2E3 reacted with the p24 but not p27 form, and was strain specific (MN and BRU reactive, not IIIB or RF) [Ovod1992]					
1099	polyclonal	Nef (66–97)	Nef (66–97 LAI)	VGFPVTPQVPLRPMTYKAAVDLSHF-LKEKGGL	no	Vaccine	human (IgG)
		Vaccine *Vector/Type:* lipopeptide *Strain:* LAI *HIV component:* Nef *Adjuvant:* QS21 **References** Pialoux2001 • 28 subjects were vaccinated with six HIV-1 peptides that were selected to be particularly rich in CTL epitopes, presented in lipopeptides with or without adjuvant QS21 – HIV-specific Ab responses were detected in 10/28, proliferative in 11/14, and CTL in 13/24 (54%) of testable volunteers – 10/28 had Ab responses to this peptide (N1), 11/24 had proliferative responses, and CTL responses were detected [Pialoux2001]					
1100	F14.11	Nef (83–88)	Nef (83–88)	AAVDLS		Vaccine	murine (IgG2aκ)
		Vaccine *Vector/Type:* peptide *HIV component:* Nef **References** De Santis1991, Chang1998 • F14.11: The MAb was made to a six aa region of Nef that is similar to a region found in thymosin alpha 1 protein – the MAb binds to the natural Nef protein [De Santis1991] • F14.11: Used as a control in a study of Nef-specific single chain Abs constructed from AG11 and EH1 [Chang1998]					
1101	31/03	Nef (83–103)	Nef (82–103 BH10)	AAVDLSHFLKEKGGLEGLIHS		Vaccine	murine
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Nef					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Schneider1991					
		• 31/03: Epitope mapped by overlapping decapeptides – mapping suggests complex epitope in this region [Schneider1991]					
1102	polyclonal	Nef (117–147)	Nef (117–147 LAI)	TQGYFPDWQNYTPGPGVRYPLTFGW-CYKLVP	no	Vaccine	human (IgG)
		Vaccine *Vector/Type:* lipopeptide *Strain:* LAI *HIV component:* Nef *Adjuvant:* QS21					
		References Pialoux2001					
		• 28 subjects were vaccinated with six HIV-1 peptides that were selected to be particularly rich in CTL epitopes, presented in lipopeptides with or without adjuvant QS21 – HIV-specific Ab responses were detected in 25/28, proliferative in 3/24, and CTL in 13/24 (54%) of testable volunteers – 20/28 had antibody responses to this particular peptide (N2), 3/24 had proliferative responses, and CTL responses were detected [Pialoux2001]					
1103	polyclonal	Nef (118–133)	Nef (118–133)	QGYFPDWQNYTPGPGV	no	Vaccine	murine (IgG)
		Vaccine *Vector/Type:* DNA *Strain:* BRU *HIV component:* Nef					
		References Tahtinen2001					
		• BALB/c mice were immunized with a pBN-vector expressing HIV-1 nef, rev, or tat genes—DNA loaded onto gold microparticles was delivered using a gene gun, and DNA dissolved in saline was given intradermally or intramuscularly—Nef gene gun immunized mice showed the strongest and most long-lasting (6 months) Ab, CTL and proliferative responses—the highest IgG1/IgG2a ratio was observed in the gene gun immunized mice—three Ab binding sites were found in Nef using peptide mapping, although some sera reacted only to complete Nef—Rev- or Tat-immunized mice did not generate an Ab response [Tahtinen2001].					
1104	polyclonal	Nef (119–168)	Nef (118–167 LAI, BRU)	GYFPDWQNYTPGPGVRYPLTFGWCY-KLVPVEPDKVEEANKGENTSLLHPV		HIV-1 infection, Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* PLG, recombinant protein *Strain:* LAI, BRU *HIV component:* Nef *Adjuvant:* PLG, complete Freund's adjuvant (CFA)					
		References Moureau2002, Maksiutov2002					
		• Nef encapsulated in poly(DL-lactide-co-glycolide) (PLG) had a more prolonged Ab response than Nef in PBS or in Freund's adjuvant (CFA), still strong after 7 months – the response was predominantly IgG1, a Th2 immune response – three linear epitopes, Nef 32-64, 118-167, and 185-205, were frequently recognized by the sera of mice immunized with NefPLG or Nef-CFA, but not after immunization with Nef in PBS, which seemed to preferentially stimulate an Ab response to conformational epitopes [Moureau2002]					
		• This epitope is similar to a fragment of the human protein Bone-derived growth factor, PLEPAKLEE, and to Hematopoietic progenitor cell antigen CD34, TSLHPVSQHG [Maksiutov2002]					
1105	F1	Nef (148–157)	Nef (148–157 IIIB)	VEPDKVEEAN			murine (IgM)
		References Fujii1993, Otake1994, Fujii1996c, Fujii1996b					
		• F1: The C-term end of Nef is accessible to Abs at the cell surface – stained IIIB/M10, but not MN/M10, cells [Otake1994, Fujii1993]					
		• F1: Insect cells expressing myristylated Nef proteins on their cell surface can induce cytolysis of unstimulated CD4+ cells – this response is not due to MHC restricted CTL activity – the cell surface of Nef expressing insect cells carry Nef that can be recognized by MAbs E7 and E9 but not F1 [Fujii1996c]					
		• F1: A carboxy-terminal domain of Nef on the cell surface induces cytolysis of CD4+ T cells [Fujii1996b]					
1106	2F2	Nef (151–170)	Nef (151–170 BRU)	DKVEEANKGENTSLLHPVSL		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Nef					
		References Ovod1992, Saito1994, Ranki1995, Maksiutov2002					
		• 2F2: Strain specific (MN and BRU reactive, not IIIB or RF) [Ovod1992]					
		• 2F2: Over-expression of Nef in astrocytes from postmortem pediatric CNS tissue [Saito1994]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 2F2: One of four antibodies used in combination to show HIV Nef protein expressed in astrocytes from 7/14 brain samples from HIV+ individuals – Nef expression associated with dementia [Ranki1995] • 2F2: This epitope is similar to a fragment of the human protein Hematopoietic progenitor cell antigen CD34, TSLHPVSQHG[Maksiutov2002] • 2F2: UK Medical Research Council AIDS reagent: EVA3067.3					
1107	E9	Nef (158–181)	Nef (158–206 IIIB)	KGENTSLLHPVSLHGMDDPEREVL			murine (IgM)
		References Fujii1993, Otake1994, Fujii1996c, Fujii1996b, Maksiutov2002 • E9: The C-term end of Nef is accessible to Abs at the cell surface – stained IIIB/M10, but not MN/M10, cells [Otake1994, Fujii1993] • E9: A carboxy-terminal domain of Nef on the cell surface induces cytolysis of CD4+ T cells [Fujii1996b] • E9: Insect cells expressing myristylated Nef proteins on their cell surface can induce cytolysis of unstimulated CD4+ cells – this response is not due to MHC restricted CTL activity – the cell surface of Nef expressing insect cells carry Nef that can be recognized by MAbs E7 and E9 but not F1 [Fujii1996c] • E9: This epitope is similar to a fragment of the human protein Hematopoietic progenitor cell antigen CD34, TSLHPVSQHG[Maksiutov2002]					
1108	3E6	Nef (161–180)	Nef (161–180 BRU)	NTSLLHPVSLHGMDDPEREV		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *Strain:* BRU *HIV component:* Nef **References** Ovod1992, Saito1994, Ranki1995, Maksiutov2002 • 3E6: Reacted with Nef from different HIV-1 strains (BRU, IIIB, RF, MN) [Ovod1992] • 3E6: Faintly cross-reactive with astrocytes of uninfected control samples [Ranki1995] • 3E6: This epitope is similar to a fragment of the human protein Hematopoietic progenitor cell antigen CD34, TSLHPVSQHG[Maksiutov2002] • 3E6: UK Medical Research Council AIDS reagent: EVA3067.4					
1109	2A3	Nef (171–190)	Nef (171–190 BRU)	HGMDDPEREVLEWRFDSRLA		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *Strain:* BRU *HIV component:* Nef **References** Ovod1992 • 2A3: Reacted with Nef from different HIV-1 strains (BRU, IIIB, MN, but not RF) [Ovod1992]					
1110	2E4	Nef (171–190)	Nef (171–190 BRU)	HGMDDPEREVLEWRFDSRLA		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *Strain:* BRU *HIV component:* Nef **References** Ovod1992 • 2EA: Reacted with Nef from different HIV-1 strains (BRU, IIIB, MN but not RF) [Ovod1992]					
1111	2H12	Nef (171–190)	Nef (171–190 BRU)	HGMDDPEREVLEWRFDSRLA		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *Strain:* BRU *HIV component:* Nef **References** Ovod1992, Saito1994, Ranki1995 • 2H12: Reacted with Nef from different HIV-1 strains (BRU, IIIB, RF, MN) [Ovod1992] • 2H12: Over-expression of Nef in astrocytes from postmortem pediatric CNS tissue [Saito1994] • 2H12: One of four antibodies used in combination to show HIV Nef protein expressed in astrocytes from 7/14 brain samples from HIV+ individuals – Nef expression associated with dementia [Ranki1995]					
1112	3A2	Nef (171–190)	Nef (171–190 BRU)	HGMDDPEREVLEWRFDSRLA		Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* recombinant protein *Strain:* BRU *HIV component:* Nef **References** Ovod1992, Saito1994, Ranki1995 • 3A2: Reacted with Nef from different HIV-1 strains (BRU, IIIB, RF, MN) [Ovod1992] • 3A2: Over-expression of Nef in astrocytes from postmortem pediatric CNS tissue [Saito1994]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 3A2: One of four antibodies used in combination to show HIV Nef protein expressed in astrocytes from 7/14 brain samples from HIV+ individuals – Nef expression associated with dementia [Ranki1995] • 3A2: UK Medical Research Council AIDS reagent: EVA3067.5					
1113	NF1A1	Nef (173–206)	Nef (173–206)	MDDPEREVLEWRFDSRLAFHHVARE-LHPEYFKNC			murine
		References Kaminchik1990 • NF1A1: Recognizes the Nef protein of the two isolates BH10 and LAV1 – low affinity [Kaminchik1990]					
1114	polyclonal	Nef (186–206)	Nef (185–205 LAI, BRU)	DSRLAFHHVARELHPEYFKNC		HIV-1 infection, Vaccine	murine (IgG1)
		Vaccine *Vector/Type:* PLG, recombinant protein *Strain:* LAI, BRU *HIV component:* Nef *Adjuvant:* PLG, complete Freund's adjuvant (CFA) **References** Moureau2002 • Nef encapsulated in poly(DL-lactide-co-glycolide) (PLG) had a more prolonged Ab response than Nef in PBS or in Freund's adjuvant (CFA), still strong after 7 months – the response was predominantly IgG1, a Th2 immune response – three linear epitopes, Nef 32-64, 118-167, and 185-205, were frequently recognized by the sera of mice immunized with NefPLG or Nef-CFA, but not after immunization with Nef in PBS, which seemed to preferentially stimulate an Ab response to conformational epitopes [Moureau2002]					
1115	E7	Nef (192–206)	Nef (192–206 IIIB)	HHVARELHPEYFKNC			murine (IgM)
		References Fujii1993, Otake1994, Fujii1996c, Fujii1996a, Fujii1996b, Fujii1996d • E7: The C-term end of Nef is accessible to Abs at the cell surface – stained IIIB/M10, but not MN/M10, cells [Otake1994, Fujii1993] • E7: Insect cells expressing myristylated Nef proteins on their cell surface can induce cytolysis of unstimulated CD4+ cells – this response is not due to MHC restricted CTL activity – the cell surface of Nef expressing insect cells carry Nef that can be recognized by MAbs E7 and E9 but not F1 [Fujii1996c] • E7: Nef forms a homomeric oligomerizing structure, and using E7 and membrane immunofluorescence or immunoelectron microscopy, was shown to clusters on the surface of HIV-1 infected CD4+ cells [Fujii1996a] • E7: A carboxy-terminal domain of Nef on the cell surface induces cytolysis of CD4+ T cells [Fujii1996b] • E7: Soluble Nef inhibits proliferation of CD4+ cells, and Nef cross-linking by MAbs may induce anti-CD4 cytocidal activity – sera from HIV+ individuals contain soluble Nef, thus this may be important for immune dysfunction and disease progression [Fujii1996d]					
1116	AE6	Nef (194–206)	Nef (LAI)	VARELHPEYFKNC		Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Nef **Ab type** C-term **Donor** Frank Jirik, Centre for Molecular Med and Therapeutics, U. B. C., Vancouver, B. C. Canada **References** Chang1998 • AE6: The light and heavy chains of three MAbs (AG11, AE6, EH1) specific to C-terminus of NEF were cloned and variable regions sequenced – the complementarity determining regions (CDR) of AG11 and AE6 were highly related (95.1% at the DNA level) and bound LAI Nef, but not SF2 Nef – EH1 bound to SF2 and LAI and cross-competed AG11 and AE6 but had a distinctive CDR (57.9% similar to AG11) – single chain Abs were constructed from AG11 and EH1 [Chang1998]					
1117	AG11	Nef (194–206)	Nef (LAI)	VARELHPEYFKNC		Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Nef **Ab type** C-term **Donor** Frank Jirik, Centre for Molecular Med and Therapeutics, U. B. C., Vancouver, B. C. Canada **References** Chang1998					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• AG11: The light and heavy chains of three MAbs (AG11, AE6, EH1) specific to C-terminus of NEF were cloned and variable regions sequenced – the complementarity determining regions (CDR) of AG11 and AE6 were highly related (95.1% at the DNA level) and bound LAI Nef, but not SF2 Nef – EH1 bound to SF2 and LAI and cross-competed AG11 and AE6 but had a distinctive CDR (57.9% similar to AG11) – single chain Abs were constructed from AG11 and EH1 and subcloned into a eukaryotic expression vector with a green fluorescent protein marker to allow intracellular expression – the single chain Abs bind Nef intracellularly and may be useful to better understand the role of Nef and as a gene therapy model [Chang1998]					
1118	EH1	Nef (194–206)	Nef (SF2)	MARELHPEYYKDC		Vaccine	murine (IgG1κ)
		Vaccine *Vector/Type:* recombinant protein *HIV component:* Nef **Ab type** C-term **Donor** Frank Jirik, Centre for Molecular Med and Therapeutics, U. B. C., Vancouver, B. C. Canada **References** Chang1998					
		• EH1: The light and heavy chains of three MAbs (AG11, AE6, EH1) specific to C-terminus of NEF were cloned and variable regions sequenced – the complementarity determining regions (CDR) of AG11 and AE6 were highly related (95.1% at the DNA level) and bound LAI Nef, but not SF2 Nef – EH1 bound to SF2 and LAI and cross-competed AG11 and AE6 but had a distinctive CDR (57.9% similar to AG11) – single chain Abs were constructed from AG11 and EH1 and subcloned into a eukaryotic expression vector with a green fluorescent protein marker to allow intracellular expression – the single chain Abs bind Nef intracellularly and may be useful to better understand the role of Nef and as a gene therapy model [Chang1998]					
1119	6.1	Nef	Nef (dis JRCSF)				murine
		References Ranki1995					
		• 6.1: Raised against CNS primary isolates, stains astrocytes more densely than other Nef MAbs – Nef expression associated with dementia [Ranki1995] • 6.1: NIAID Repository number 1123 [Ranki1995]					
1120	NF2B2	Nef	Nef (20–78 BH10)			Vaccine	murine
		Vaccine *Vector/Type:* recombinant protein *Strain:* BH10 *HIV component:* Nef **References** Kaminchik1990					
		• NF2B2: Recognizes the Nef protein of the two isolates BH10 and LAV1 [Kaminchik1990] • NF2B2: NIH AIDS Research and Reference Reagent Program: 456					
1121	NF3A3	Nef	Nef (20–78 BH10)			Vaccine	murine
		Vaccine *Vector/Type:* recombinant protein *Strain:* BH10 *HIV component:* Nef **References** Kaminchik1990					
		• NF3A3: Recognizes the Nef protein of the two isolates BH10 and LAV1 – low affinity [Kaminchik1990]					
1122	NF8B4	Nef	Nef (BH10)			Vaccine	murine
		Vaccine *Vector/Type:* recombinant protein *Strain:* BH10 *HIV component:* Nef **References** Kaminchik1990					
		• NF8B4: Does not recognize Nef CNBr cleavage products – recognizes intact BH10 Nef but not LAV1 Nef [Kaminchik1990]					
1123	AE6	Nef	Nef				murine
		Ab type C-term **Donor** James Hoxie, Div of AIDS, NIAID, NIH **References** Greenway1994, Tornatore1994					
		• AE6: NIH AIDS Research and Reference Reagent Program: 709					

IV-C-16 HIV-1 Antibodies

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
1124	polyclonal	HIV-1				HIV-1 infection	human
		References Fournier2002b					
		• Purified B lymphocytes secret only a fraction of Ig and anti-HIV-1 Ab compared with unfractionated cells because monocytes and natural killer cells enhance both secretions by cell-to-cell contacts, involving adhesion and CD27, CD80 costimulatory molecules and IL-6 – cell-to-cell contacts and soluble factors induce maturation of activated B cells in vitro to allow prolonged survival and terminal differentiation [Fournier2002b]					
1125	polyclonal	HIV-1				HIV-1 infection	human
		References Fournier2002a					
		• An early and sustained fall in plasma viral load to below detection was observed in 17 HAART responders while HIV-1 RNA remained detectable in 13 incomplete responders – HIV-1 specific Ab secretion decreased in parallel with plasma viral load – HIV-1 specific Abs became negative in only six responders, and was correlated with greater increases of CD4 T-cell counts and higher levels of HIV-specific IgA secretion at baseline – persistent immune activation may be due to residual HIV antigen [Fournier2002a]					
1126	polyclonal	HIV-1				HIV-1 infection	human
		References Subbramanian2002					
		• Sera from 39 patients were used to study the relative prevalence of neutralizing Abs (NAbs), ADCC-Abs and enhancing Abs – 69% of the sera were positive for NAbs but only 39% could neutralize in the presence of complement – 60% had ADCC Abs – 72% mediated the enhancement of infection in the presence of complement [Subbramanian2002]					
1127	polyclonal	HIV-1				HIV-1 infection	human (IgA, IgG1)
		References Battle-Miller2002					
		• In a study of HIV-1 infected women, ADCC Abs were detected in 16% (12/51) of cervicovaginal fluids, and 56% (25/45) of serum samples – 3 women had ADCC in cervical lavage fluids, but not sera, suggesting local production [Battle-Miller2002]					
1128	polyclonal	HIV-1				HIV-1 infection	human (IgA2, IgA1, IgM)
		References Wu2002					
		• IgA1 accounted for the majority of anti-HIV-1 IgA in the saliva in HIV-1 infected individuals – there was no anti-gp41 IgA in saliva, in contrast to plasma – lower levels of IgA and IgM were found in saliva than in plasma [Wu2002]					
1129	polyclonal	HIV-1			P	HIV-1 infection	human
		References Hioe1997a					
		• Four primary isolates showed distinct patterns of sensitivity to neutralization by polyclonal sera or plasma and MAbs – BZ167 was the only isolate inhibited by all polyclonal sera and plasma tested, and was also neutralized by 8/17 MAbs, in particular anti-V3 loop (419-D, 447-52D, 782-D, and 838-D), anti-CD4bd (559/64-D, 654-D and 830-D and a cluster II of gp41 directed MAb (98-6) – isolates 92HT593 and 91US056 were neutralized by V3 loop (419-D, and 447-52D)and cluster II gp41 (98-6) MAbs at higher concentrations – US4 was neutralized by some of the polyclonal sera/plasma tested and not at all by MAbs individually or by a cocktail of ten MAbs consisting of 419-D, 447-52D, 782-D, 838-D, 559/64-D, 654-D, 450-D, 670-D, 1281-D and 98-6 [Hioe1997a]					
1130	polyclonal	HIV-1			no	HIV-1 infection	human (IgA, IgG)
		References Oelemann2002					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• A urine based commercial EIA kit from Calypte Biomedical Corporation, Berkeley, CA was found to work well as a primary screening for HIV in Brazilian samples – 76 HIV+ samples were correctly identified (100% sensitivity), and 278/284 negative samples 97.9% specificity [Oelemann2002]					
1131	polyclonal	HIV-1	HIV-1		no	HIV-1 infection	human (IgE)
		References Secord1996, Pellegrino2002					
		• HIV-specific IgE found in clinically healthy HIV-1 infected children [Secord1996]					
		• Pediatric long term survivors (LTS) have been found to carry HIV-1 specific IgE – serum from these children inhibit HIV-1 production in culture, but this inhibition did not seem to be due to neutralization, rather due to a cytoxic event – serum lost the HIV-1 inhibitory effect when depleted of IgE [Pellegrino2002]					

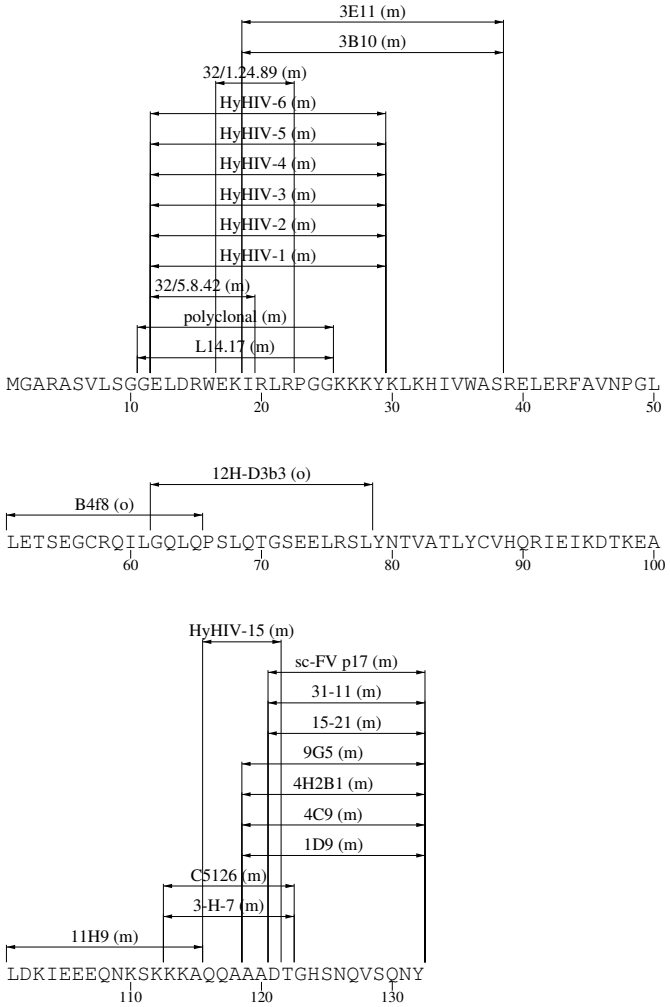
IV-D Maps of MAb Locations Plotted by Protein

Linear epitopes less than twenty-two amino acids long are shown with their antibody ID and the experimental species.

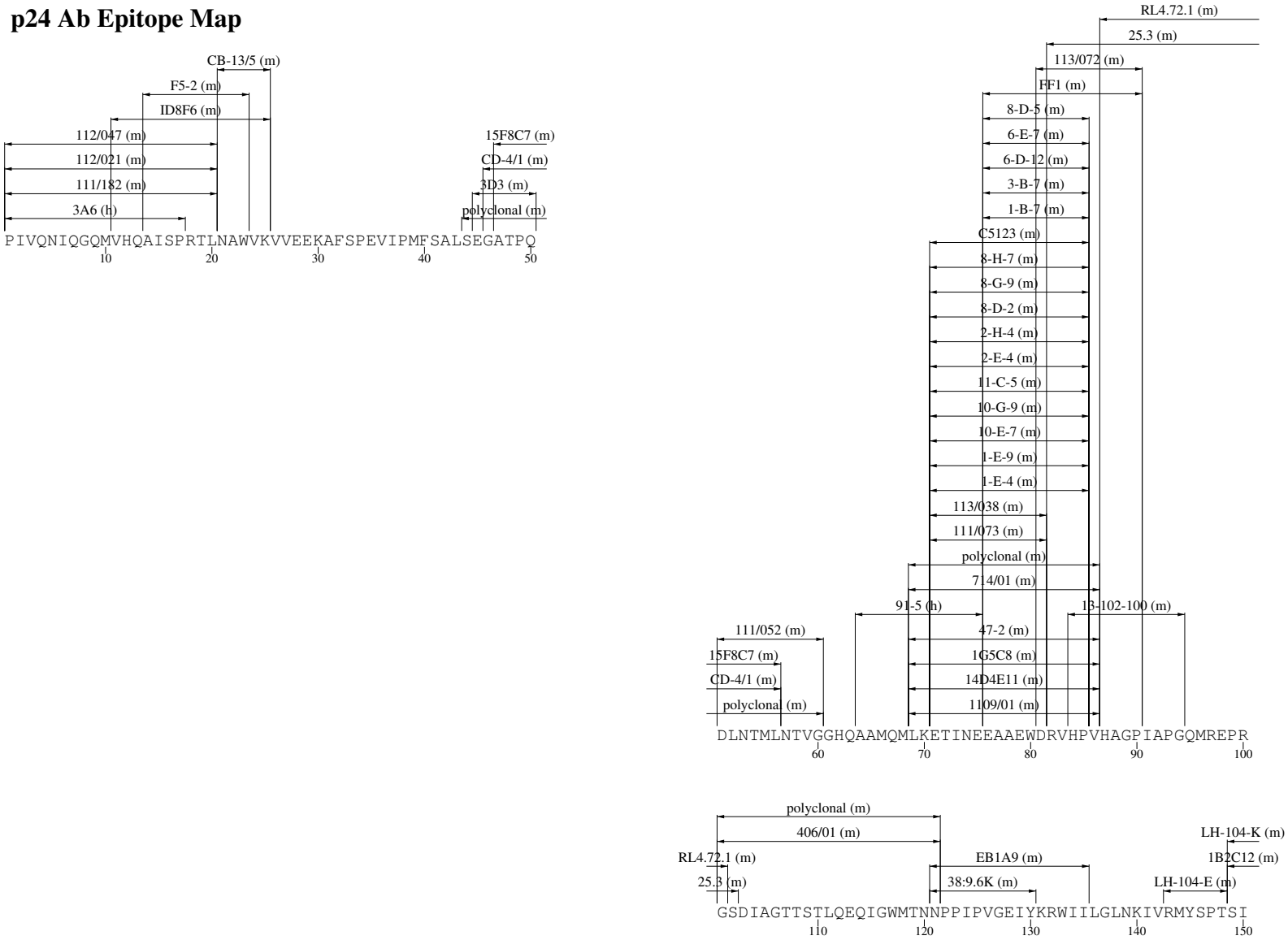
Key	Species
h	human
p	non-human primate
m	murine
o	other

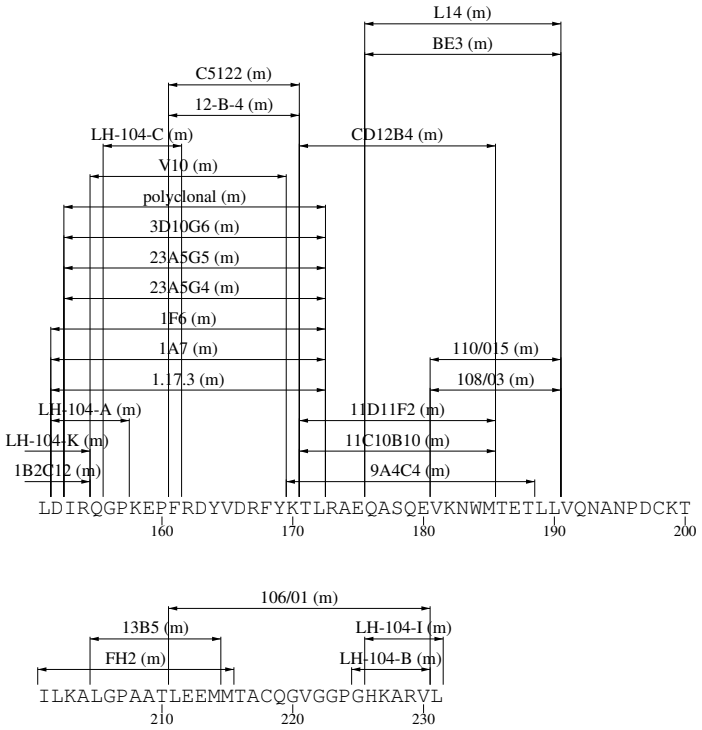
Table IV-D.1: The species for which the epitopes react

IV-D-1 p17 Ab Epitope Map

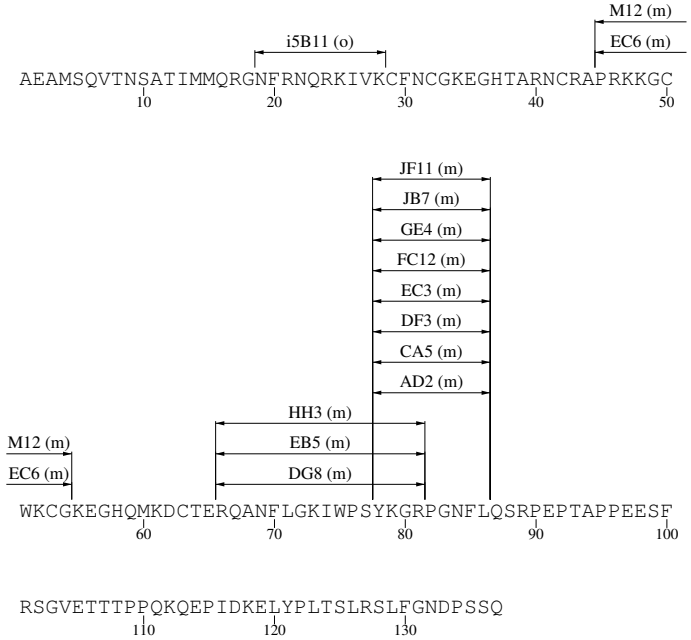


IV-D-2 p24 Ab Epitope Map

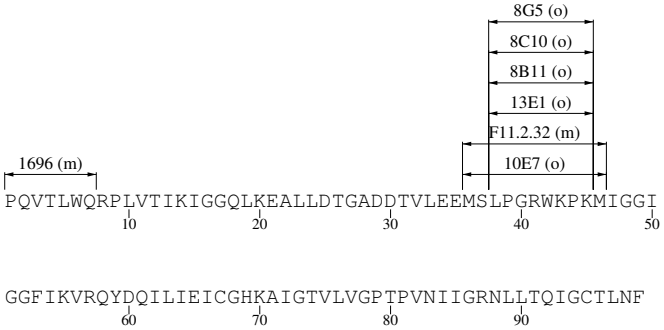




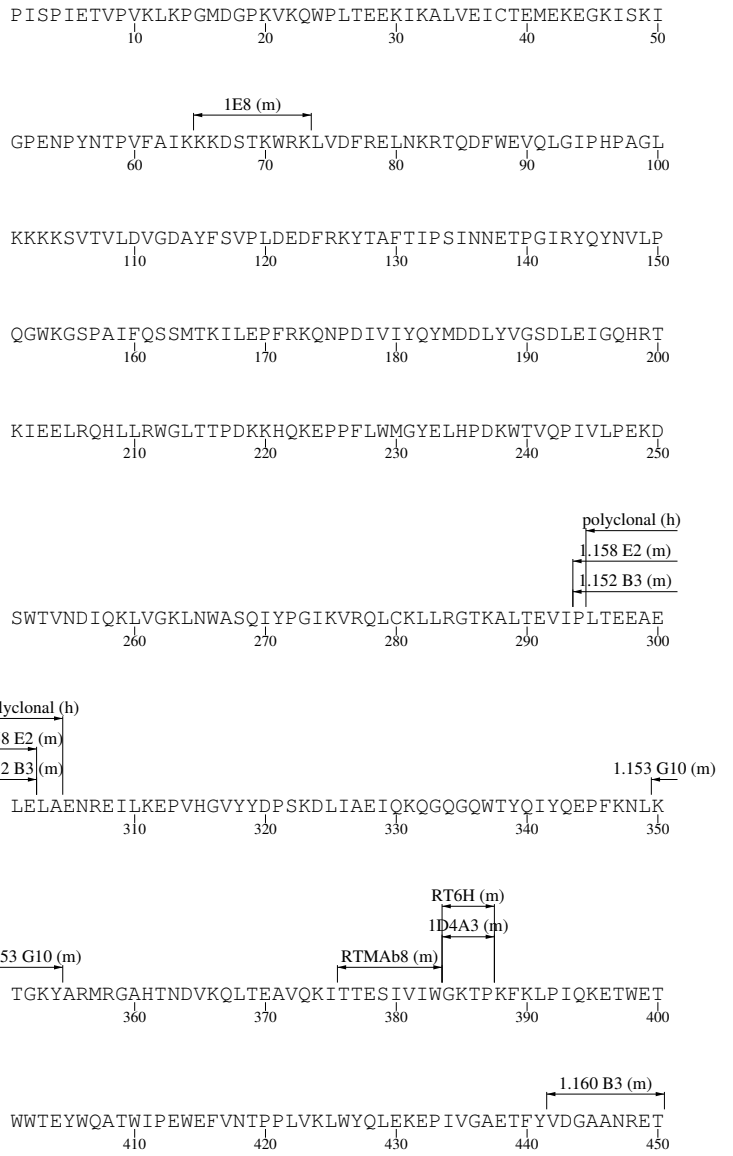
IV-D-3 p2p7p1p6 Ab Epitope Map

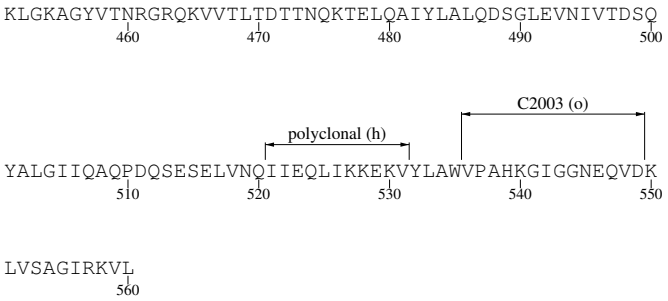


IV-D-4 Protease Ab Epitope Map

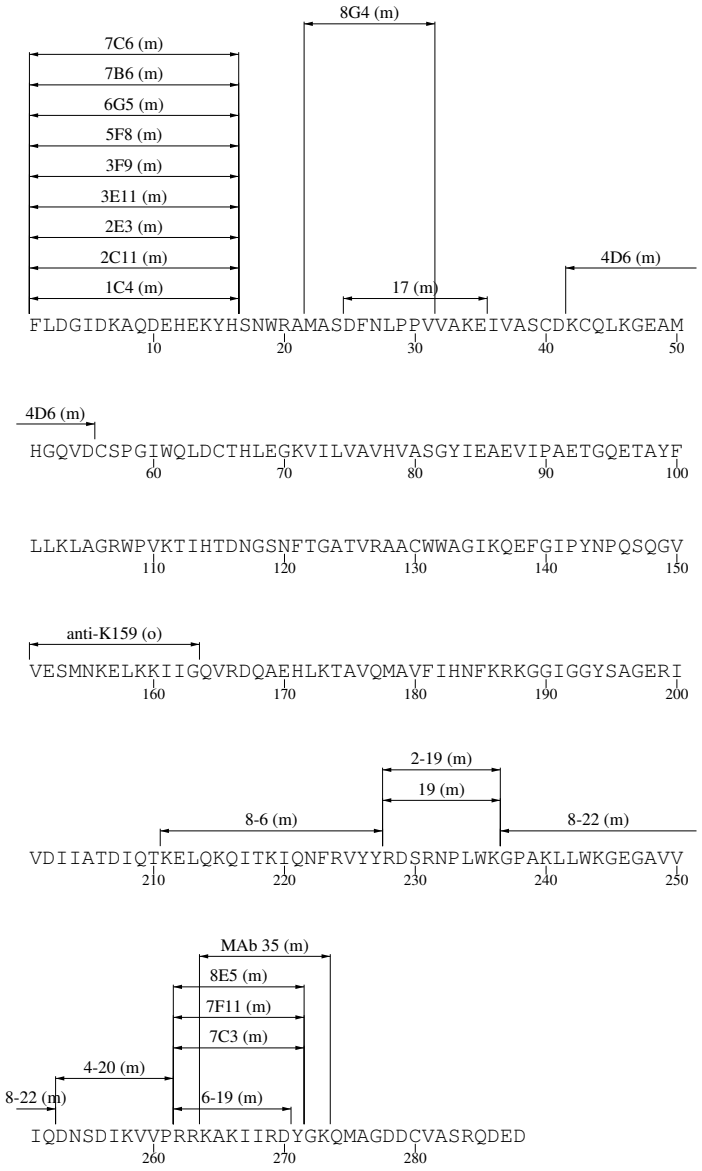


IV-D-5 RT Ab Epitope Map

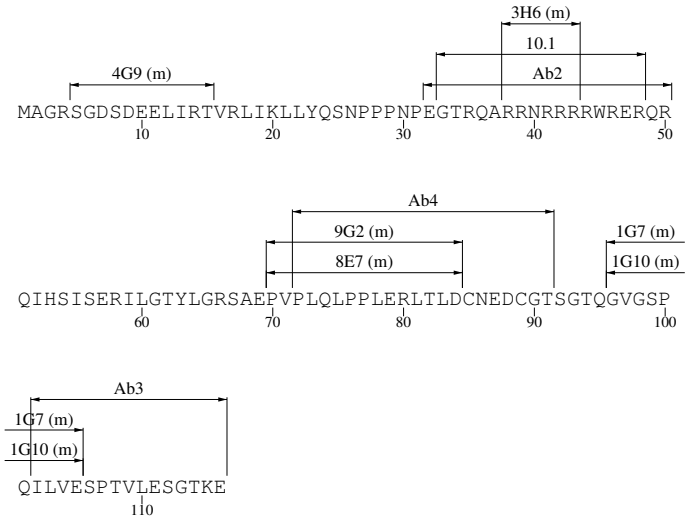




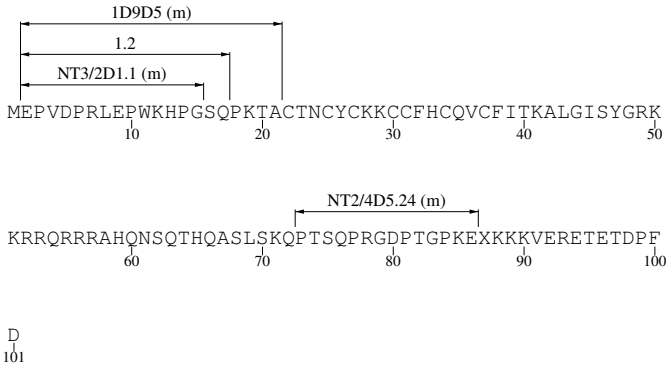
IV-D-6 Integrase Ab Epitope Map



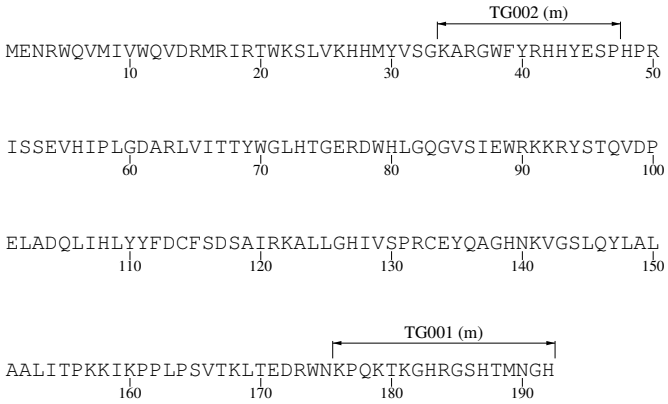
IV-D-7 Rev Ab Epitope Map



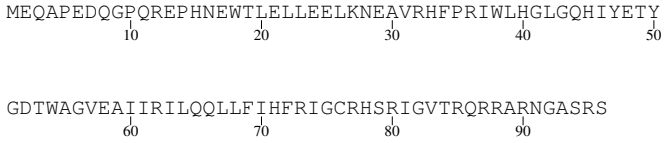
IV-D-8 Tat Ab Epitope Map



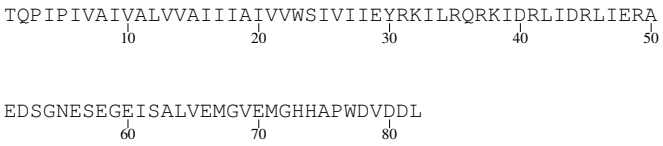
IV-D-9 Vif Ab Epitope Map



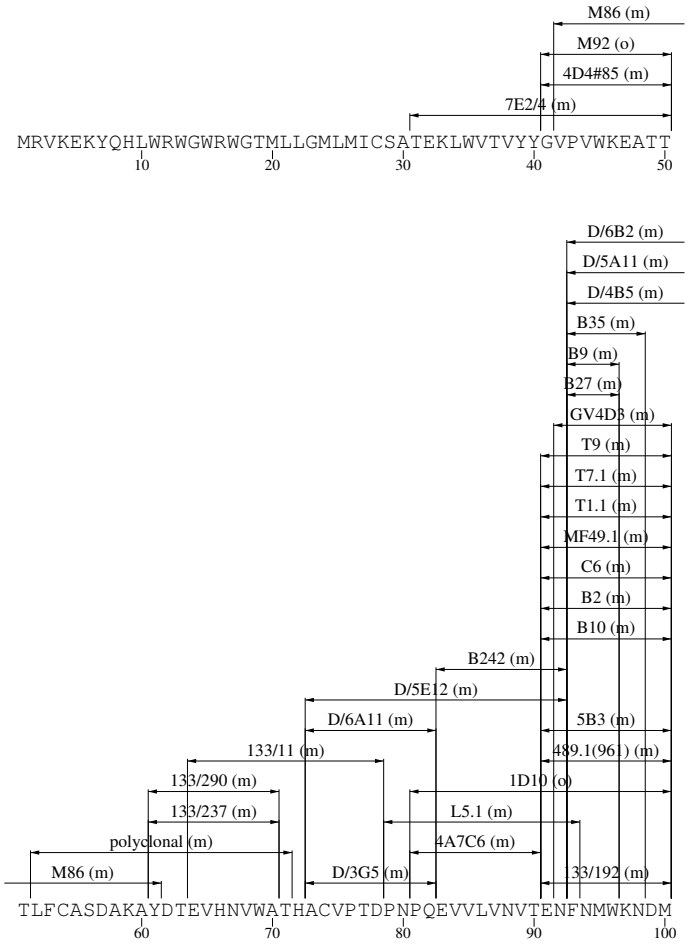
IV-D-10 Vpr Ab Epitope Map



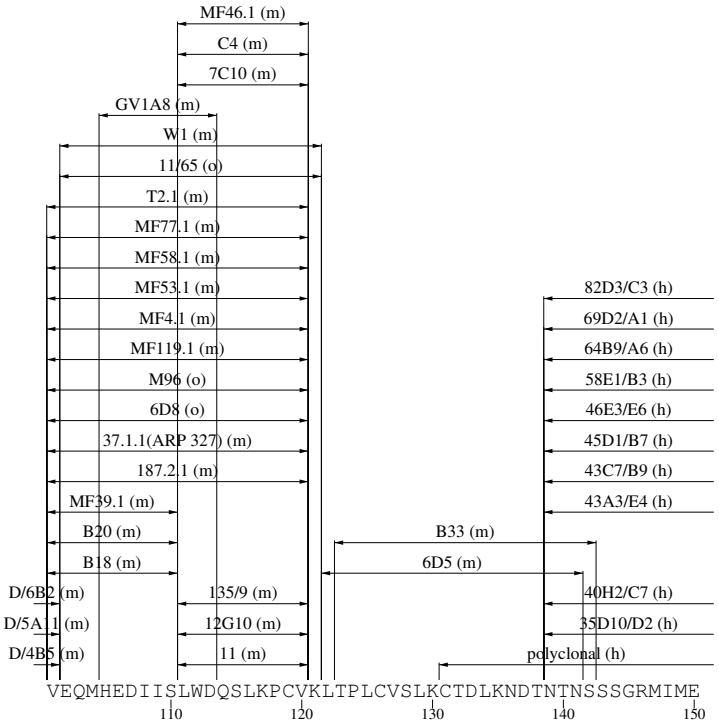
IV-D-11 Vpu Ab Epitope Map

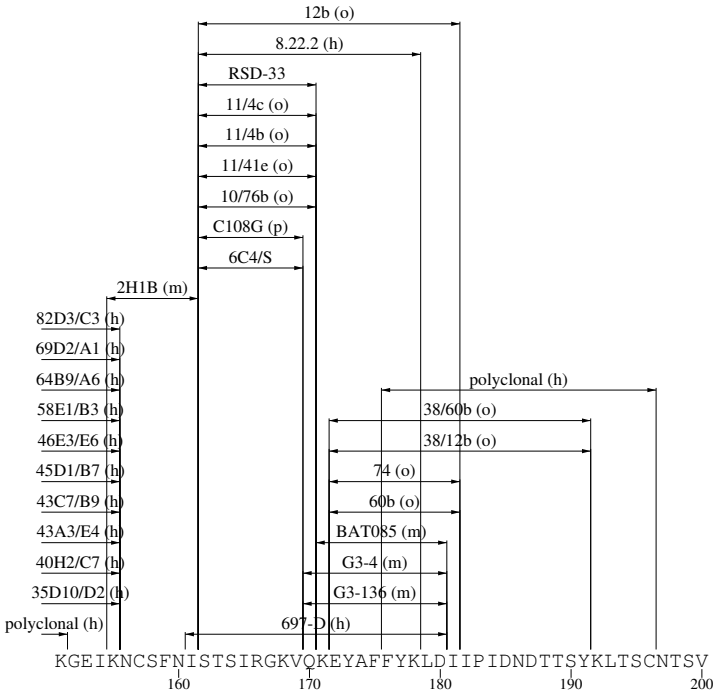


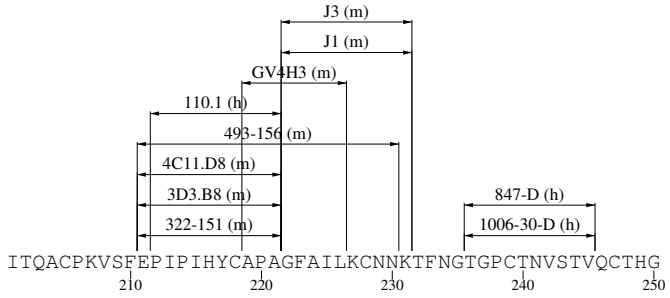
IV-D-12 gp160 Ab Epitope Map



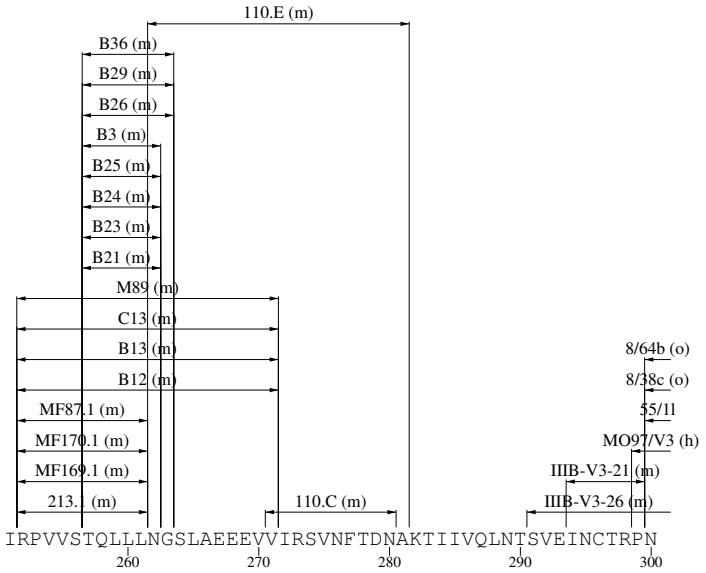
B Cell

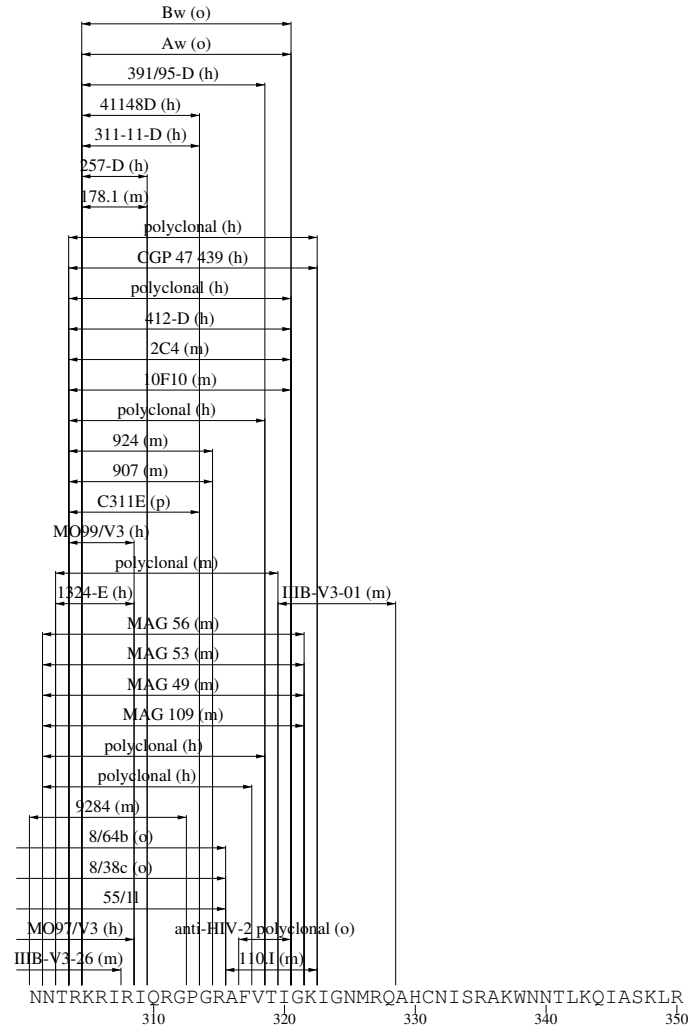

MF46.1 (m)
C4 (m)
7C10 (m)
GV1A8 (m)
W1 (m)
11/65 (o)
T2.1 (m)
MF77.1 (m)
MF58.1 (m)
MF53.1 (m)
MF4.1 (m)
MF119.1 (m)
M96 (o)
6D8 (o)
37.1.1(ARP 327) (m)
187.2.1 (m)
MF39.1 (m)
B20 (m)
B18 (m)
D/6B2 (m)
D/5A1.1 (m)
D/4B5 (m)
135/9 (m)
12G10 (m)
11 (m)
B33 (m)
6D5 (m)
82D3/C3 (h)
69D2/A1 (h)
64B9/A6 (h)
58E1/B3 (h)
46E3/E6 (h)
45D1/B7 (h)
43C7/B9 (h)
43A3/E4 (h)
40H2/C7 (h)
35D10/D2 (h)
polyclonal (h)
VEQMHEDIISLWDQSLKPCVKLTPLCVSLKCTDLKNDTNTNSSSGRMIME
110
120
130
140
150


12b (o)
8.22.2 (h)
RSD-33
11/4c (o)
11/4b (o)
11/41e (o)
10/76b (o)
C108G (p)
6C4/S
2H1B (m)
82D3/C3 (h)
69D2/A1 (h)
64B9/A6 (h)
58E1/B3 (h)
46E3/E6 (h)
45D1/B7 (h)
43C7/B9 (h)
43A3/E4 (h)
40H2/C7 (h)
35D10/D2 (h)
polyclonal (h)
polyclonal (h)
38/60b (o)
38/12b (o)
74 (o)
60b (o)
BAT085 (m)
G3-4 (m)
G3-136 (m)
697-D (h)
KGEIKNCSFNISTSIRGKVQKEYAFFYKLDIIPIDNDTTSYKLTSCNTSV
160
170
180
190
200

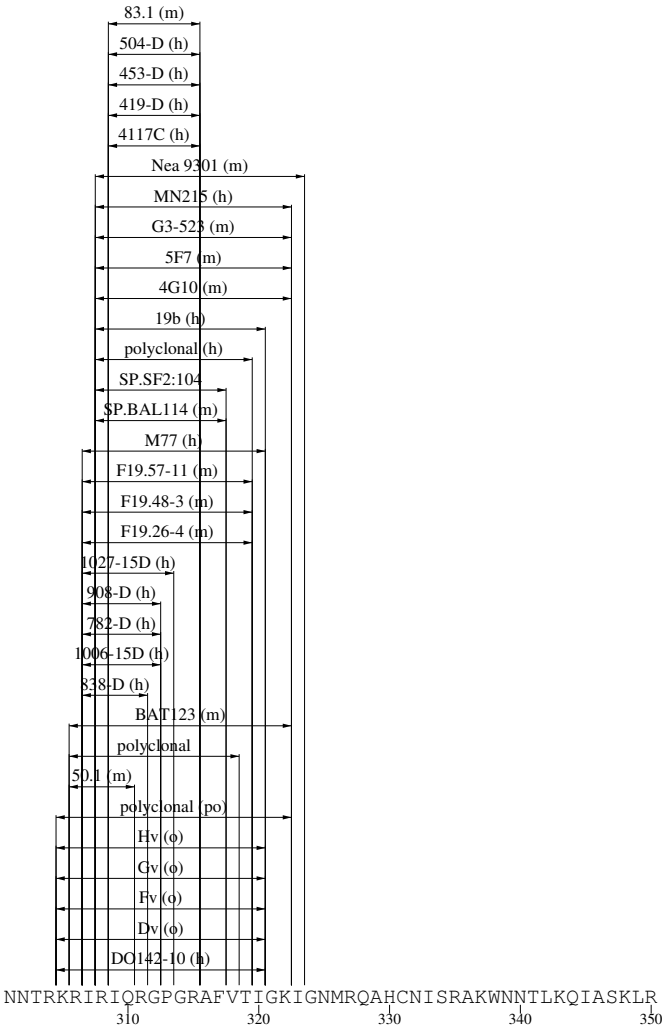

J3 (m)
J1 (m)
GV4H3 (m)
110.1 (h)
493-156 (m)
4C11.D8 (m)
3D3.B8 (m)
322-151 (m)
847-D (h)
1006-30-D (h)
ITQACPKVSFEPIPIHYCAPAGFAILKCNNKTFNGTGPCTNVSTVQCTHG
210
220
230
240
250

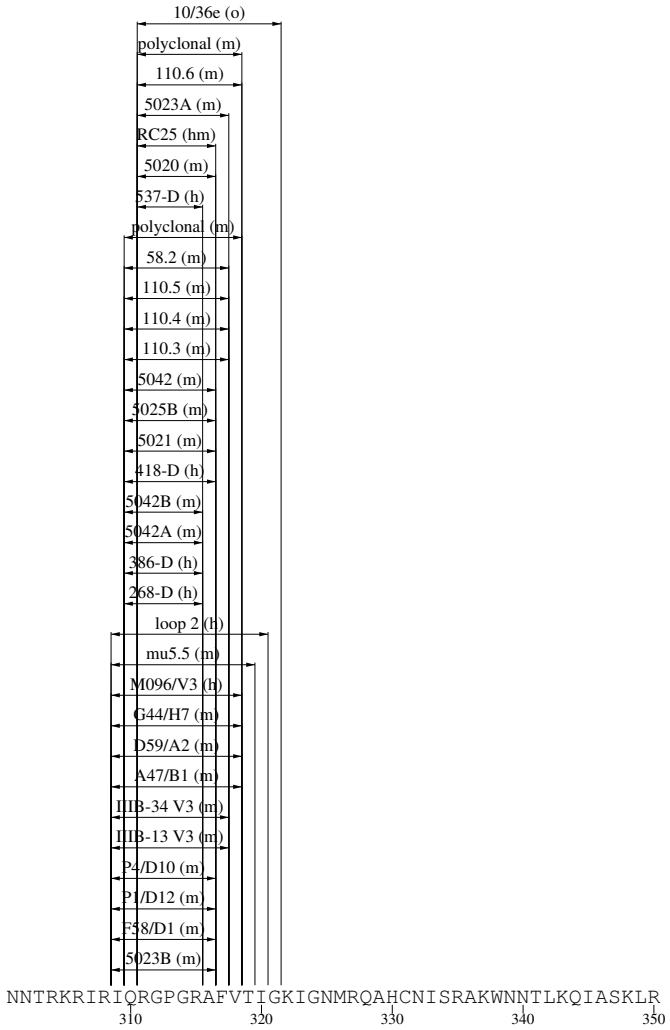
B Cell

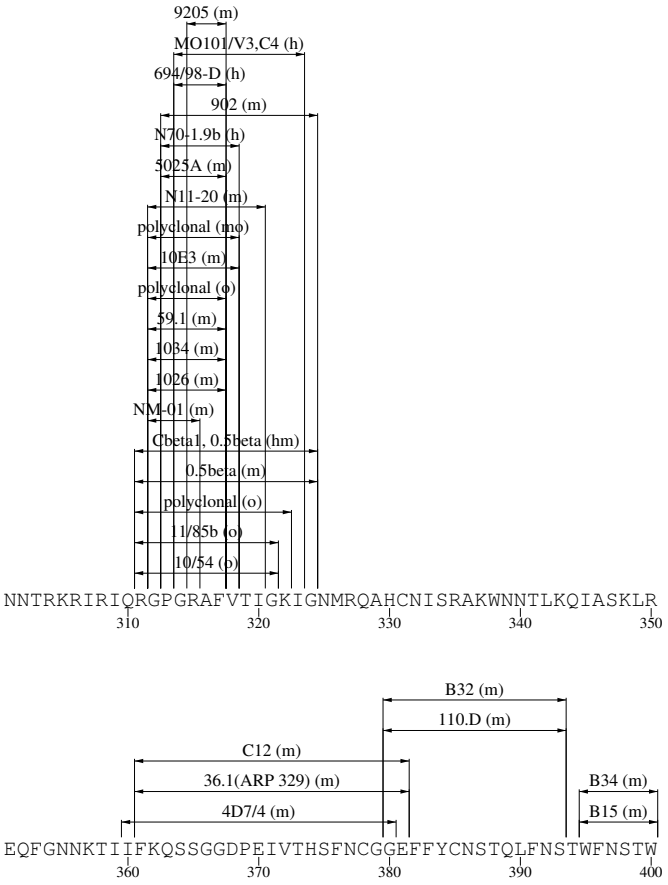

110.E (m)
B36 (m)
B29 (m)
B26 (m)
B3 (m)
B25 (m)
B24 (m)
B23 (m)
B21 (m)
M89 (m)
C13 (m)
B13 (m)
B12 (m)
MF87.1 (m)
MF170.1 (m)
MF169.1 (m)
213.1 (m)
110.C (m)
8/64b (o)
8/38c (o)
55/11
MO97/V3 (h)
IIIB-V3-21 (m)
IIIB-V3-26 (m)
IRPVVSTQLLLNGSLAEEEVVIRSVNFTDNAKTIIVQLNTSVEINCTRPN
260
270
280
290
300

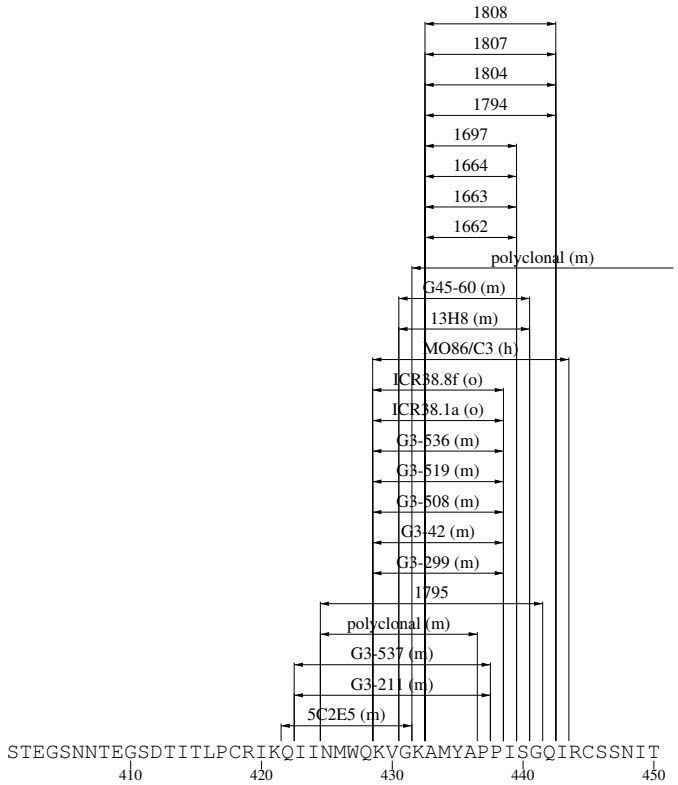

Bw (o)
Aw (o)
391/95-D (h)
41148D (h)
311-11-D (h)
257-D (h)
178.1 (m)
polyclonal (h)
CGP 47 439 (h)
polyclonal (h)
412-D (h)
2C4 (m)
10F10 (m)
polyclonal (h)
924 (m)
907 (m)
C311E (p)
MO99/V3 (h)
polyclonal (m)
1324-E (h)
IIIB-V3-01 (m)
MAG 56 (m)
MAG 53 (m)
MAG 49 (m)
MAG 109 (m)
polyclonal (h)
polyclonal (h)
9284 (m)
8/64b (o)
8/38c (o)
55/11
MO97/V3 (h)
anti-HIV-2 polyclonal (o)
IIIB-V3-26 (m)
110.I (m)
NNTRKRIRIQRGPGRAFVTIGKIGNMRQAHCNISRAKWNNTLKQIASKLR
310
320
330
340
350

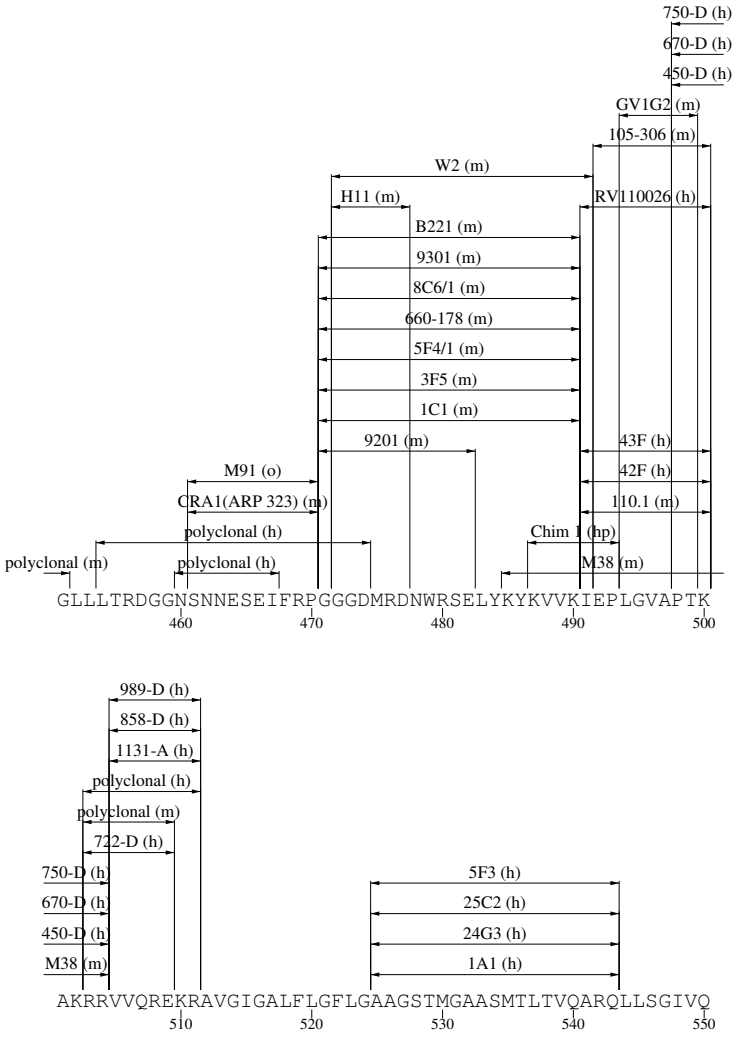
B Cell

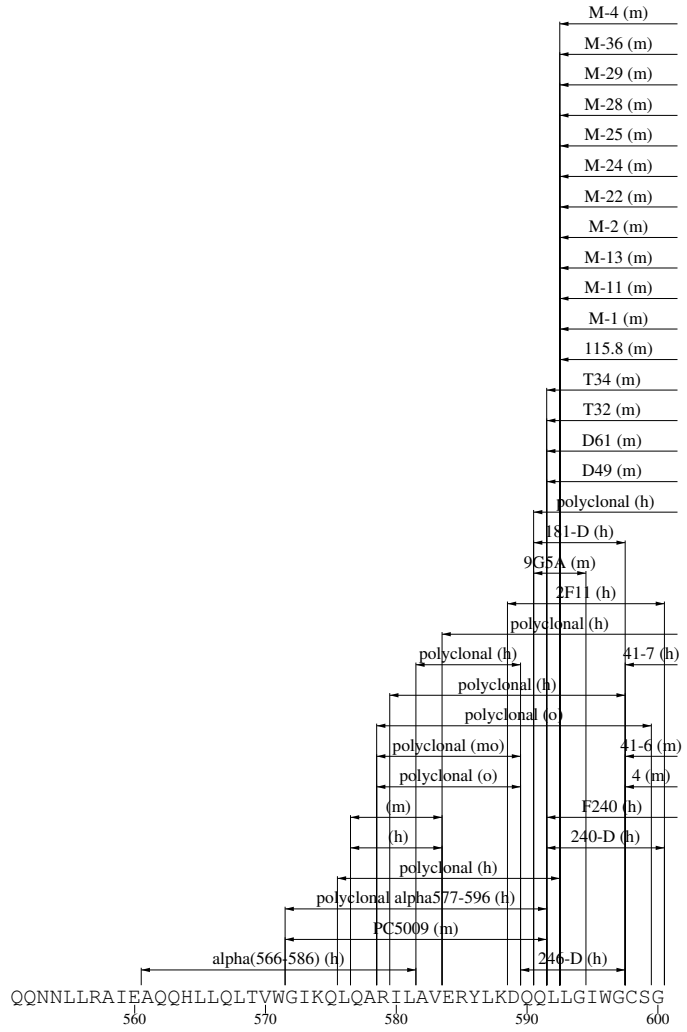

83.1 (m)
504-D (h)
453-D (h)
419-D (h)
4117C (h)
Nea 9301 (m)
MN215 (h)
G3-523 (m)
5F7 (m)
4G10 (m)
19b (h)
polyclonal (h)
SP.SF2:104
SP.BAL114 (m)
M77 (h)
F19.57-11 (m)
F19.48-3 (m)
F19.26-4 (m)
1027-15D (h)
908-D (h)
782-D (h)
1006-15D (h)
838-D (h)
BAT123 (m)
polyclonal
50.1 (m)
polyclonal (po)
Hv (o)
Gv (o)
Fv (o)
Dv (o)
DO142-10 (h)
NNTRKRIRIQRGPGRAFVTIGKIGNMRQAHCNISRAKWNNTLKQIASKLR
310
320
330
340
350

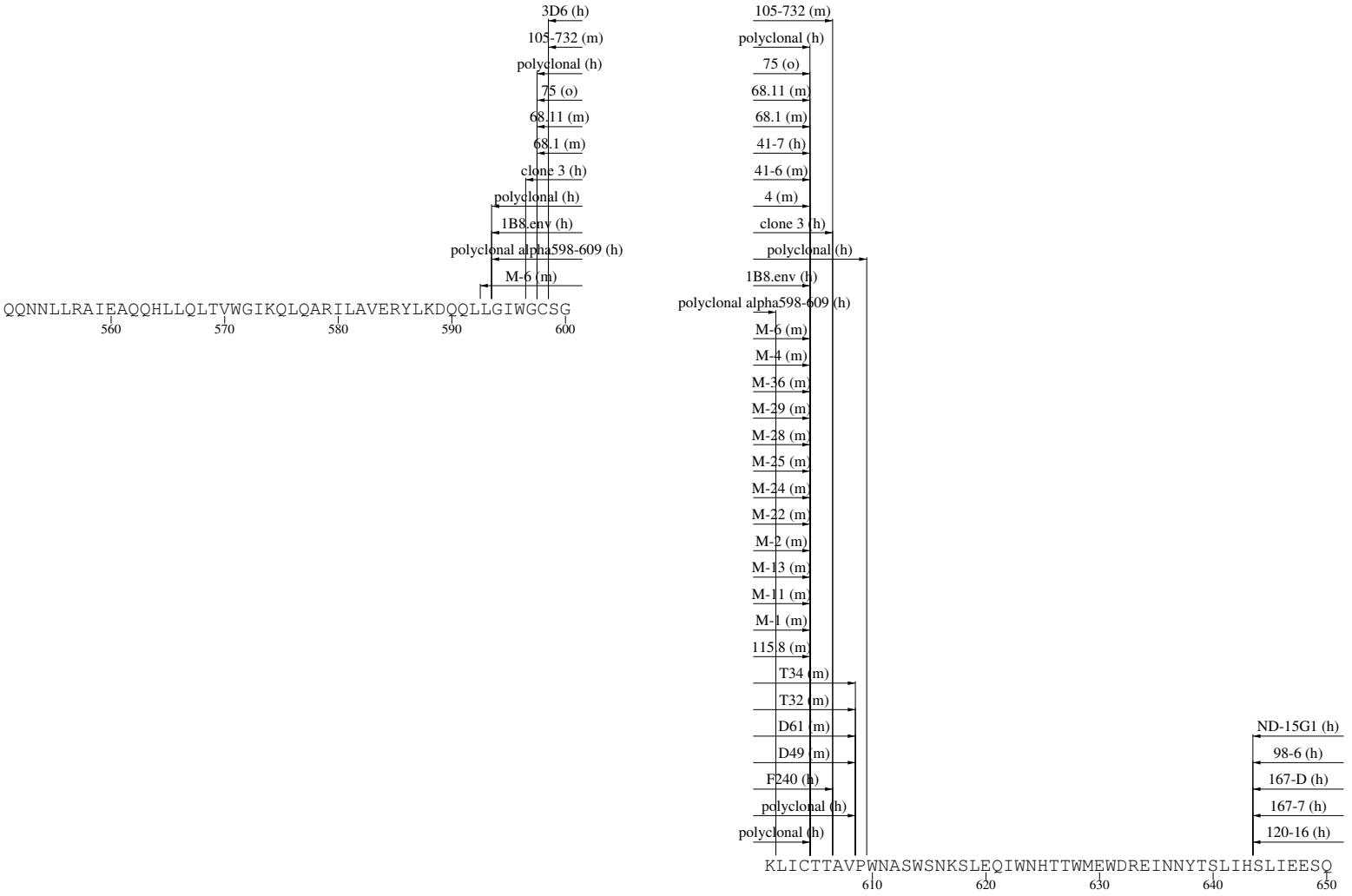

10/36e (o)
polyclonal (m)
110.6 (m)
5023A (m)
RC25 (hm)
5020 (m)
537-D (h)
polyclonal (m)
58.2 (m)
110.5 (m)
110.4 (m)
110.3 (m)
5042 (m)
5025B (m)
5021 (m)
418-D (h)
5042B (m)
5042A (m)
386-D (h)
268-D (h)
loop 2 (h)
mu5.5 (m)
M096/V3 (h)
G44/H7 (m)
D59/A2 (m)
A47/B1 (m)
IIIB-34 V3 (m)
IIIB-13 V3 (m)
P4/D10 (m)
P1/D12 (m)
F58/D1 (m)
5023B (m)
NNTRKRIRIQRGPGRAFVTIGKIGNMRQAHCNISRAKWNNTLKQIASKLR
310
320
330
340
350


9205 (m)
MO101/V3,C4 (h)
694/98-D (h)
902 (m)
N70-1.9b (h)
5025A (m)
N11-20 (m)
polyclonal (mo)
10E3 (m)
polyclonal (ϕ)
59.1 (m)
1084 (m)
1026 (m)
NM-01 (m)
Cbeta1, 0.5beta (hm)
0.5beta (m)
polyclonal (o)
11/85b (o)
10/54 (o)
NNTRKRIRIQRGPGRAFVTIGKIGNMRQAHCNISRAKWNNTLKQIASKLR
310
320
330
340
350
B32 (m)
110.D (m)
C12 (m)
36.1(ARP 329) (m)
4D7/4 (m)
B34 (m)
B15 (m)
EQFGNNKTIIFKQSSGGDPEIVTHSFNCGGEFFYCNSTQLFNSTWFNSTW
360
370
380
390
400

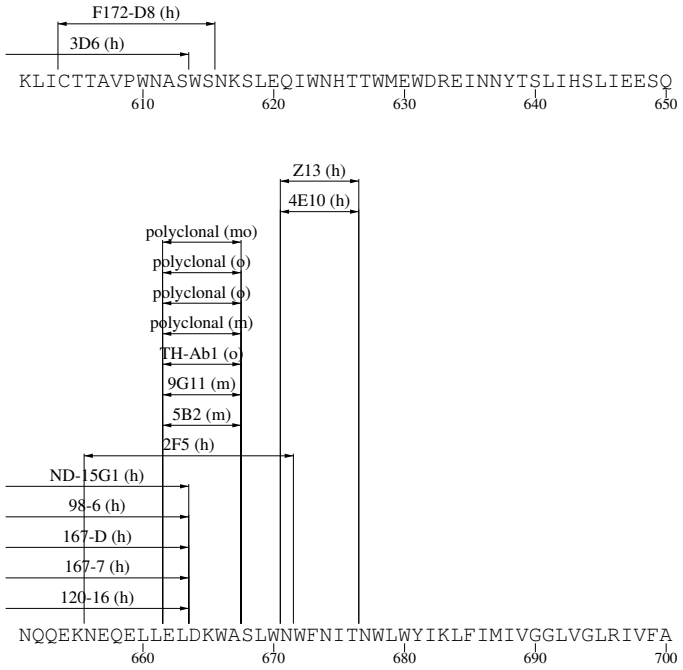

1808
1807
1804
1794
1697
1664
1663
1662
polyclonal (m)
G45-60 (m)
13H8 (m)
MO86/C3 (h)
ICR38.8f (o)
ICR38.1a (o)
G3-536 (m)
G3-519 (m)
G3-508 (m)
G3-42 (m)
G3-299 (m)
1795
polyclonal (m)
G3-537 (m)
G3-211 (m)
5C2E5 (m)
STEGSNNTEGSDTITLPCRIKQIINMWQKVGKAMYAPPISGQIRCSSNIT
410
420
430
440
450


750-D (h)
670-D (h)
450-D (h)
GV1G2 (m)
105-306 (m)
W2 (m)
H11 (m)
RV110026 (h)
B221 (m)
9301 (m)
8C6/1 (m)
660-178 (m)
5F4/1 (m)
3F5 (m)
1C1 (m)
9201 (m)
43F (h)
M91 (o)
42F (h)
CRA1(ARP 323) (m)
110.1 (m)
polyclonal (h)
Chim 1 (hp)
polyclonal (m)
polyclonal (h)
M38 (m)
GLLLTRDGGNSNNESEIFRPGGGDMRDNWRSELYKYKVVKIEPLGVAPTK
460
470
480
490
500
989-D (h)
858-D (h)
1131-A (h)
polyclonal (h)
polyclonal (m)
722-D (h)
750-D (h)
670-D (h)
450-D (h)
M38 (m)
5F3 (h)
25C2 (h)
24G3 (h)
1A1 (h)
AKRRVVQREKRAVGIGALFLGFLGAAGSTMGAASMTLTVQARQLLSGIVQ
510
520
530
540
550


M-4 (m)
M-36 (m)
M-29 (m)
M-28 (m)
M-25 (m)
M-24 (m)
M-22 (m)
M-2 (m)
M-13 (m)
M-11 (m)
M-1 (m)
115.8 (m)
T34 (m)
T32 (m)
D61 (m)
D49 (m)
polyclonal (h)
181-D (h)
9G5A (m)
2F11 (h)
polyclonal (h)
polyclonal (h)
41-7 (h)
polyclonal (h)
polyclonal (o)
polyclonal (mo)
41-6 (m)
polyclonal (o)
4 (m)
(m)
F240 (h)
(h)
240-D (h)
polyclonal (h)
polyclonal alpha577-596 (h)
PC5009 (m)
alpha(566-586) (h)
246-D (h)
QQNNLLRAIEAQQHLLQLTVWGIKQLQARILAVERYLKDQQLLGIWGCSG
560
570
580
590
600


3D6 (h)
105-732 (m)
polyclonal (h)
75 (o)
68.11 (m)
68.1 (m)
clone 3 (h)
polyclonal (h)
1B8.env (h)
polyclonal alpha598-609 (h)
M-6 (m)
QQNNLLRAIEAQQHLLQLTVWGIKQLQARILAVERYLKDQQLLGIWGCSG
560
570
580
590
600
105-732 (m)
polyclonal (h)
75 (o)
68.11 (m)
68.1 (m)
41-7 (h)
41-6 (m)
4 (m)
clone 3 (h)
polyclonal (h)
1B8.env (h)
polyclonal alpha598-609 (h)
M-6 (m)
M-4 (m)
M-36 (m)
M-29 (m)
M-28 (m)
M-25 (m)
M-24 (m)
M-22 (m)
M-2 (m)
M-13 (m)
M-11 (m)
M-1 (m)
115.8 (m)
T34 (m)
T32 (m)
D61 (m)
D49 (m)
F240 (h)
polyclonal (h)
polyclonal (h)
ND-15G1 (h)
98-6 (h)
167-D (h)
167-7 (h)
120-16 (h)
KLICTTAVPWNASWSNKSLEQIWNHTTWMEWDREINNYTSLIHSLIEESQ
610
620
630
640
650

B Cell


F172-D8 (h)
3D6 (h)
KLICTTAVPWNASWSNKSLEQIWNHTTWMEWDREINNYTSLIHSLIEESQ
610
620
630
640
650
Z13 (h)
4E10 (h)
polyclonal (mo)
polyclonal (ϕ)
polyclonal (ϕ)
polyclonal (m)
TH-Ab1 (o)
9G11 (m)
5B2 (m)
2F5 (h)
ND-15G1 (h)
98-6 (h)
167-D (h)
167-7 (h)
120-16 (h)
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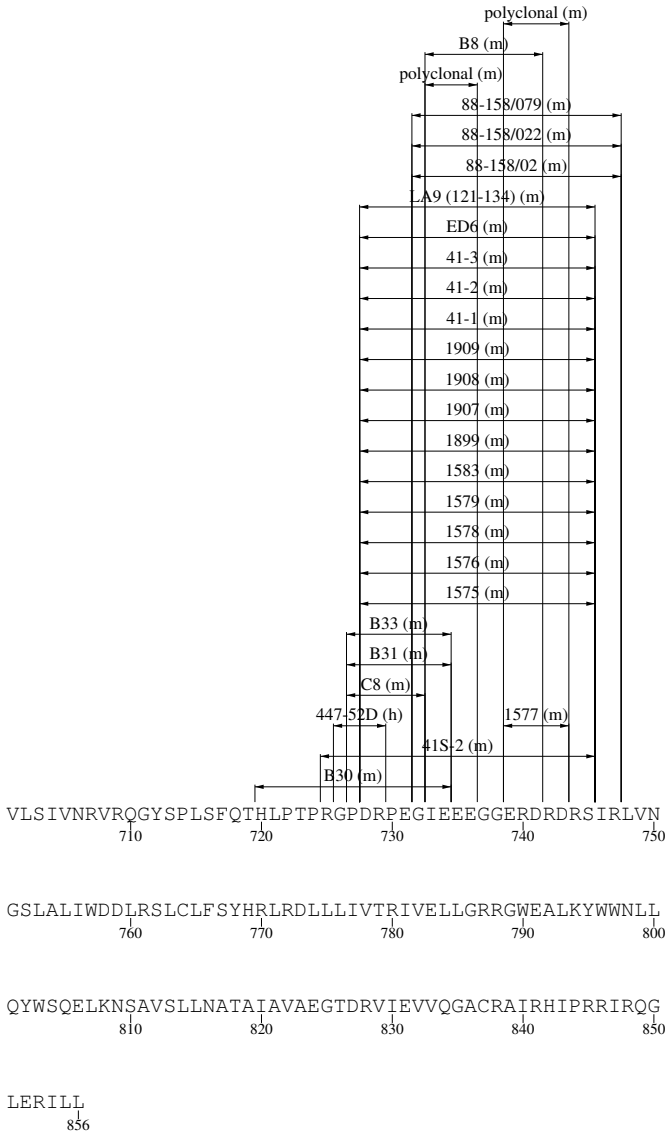
660
670
680
690
700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B8 (m)
polyclonal (m)
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88-158/022 (m)
88-158/02 (m)
LA9 (121-134) (m)
ED6 (m)
41-3 (m)
41-2 (m)
41-1 (m)
1909 (m)
1908 (m)
1907 (m)
1899 (m)
1583 (m)
1579 (m)
1578 (m)
1576 (m)
1575 (m)
B33 (m)
B31 (m)
C8 (m)
447-52D (h)
1577 (m)
41S-2 (m)
B30 (m)
VLSIVNRVRQGYSPLSFQTHLPTPRGPDRPEGIEEEGGERDRDRSIRLVN
710
720
730
740
750
GSLALIWDDLRSLCLFSYHRLRDLLLIVTRIVELLGRRGWEALKYWWNLL
760
770
780
790
800
QYWSQELKNSAVSLLNATAIAVAEGTDRVIEVVQGACRAIRHIPRRIRQG
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820
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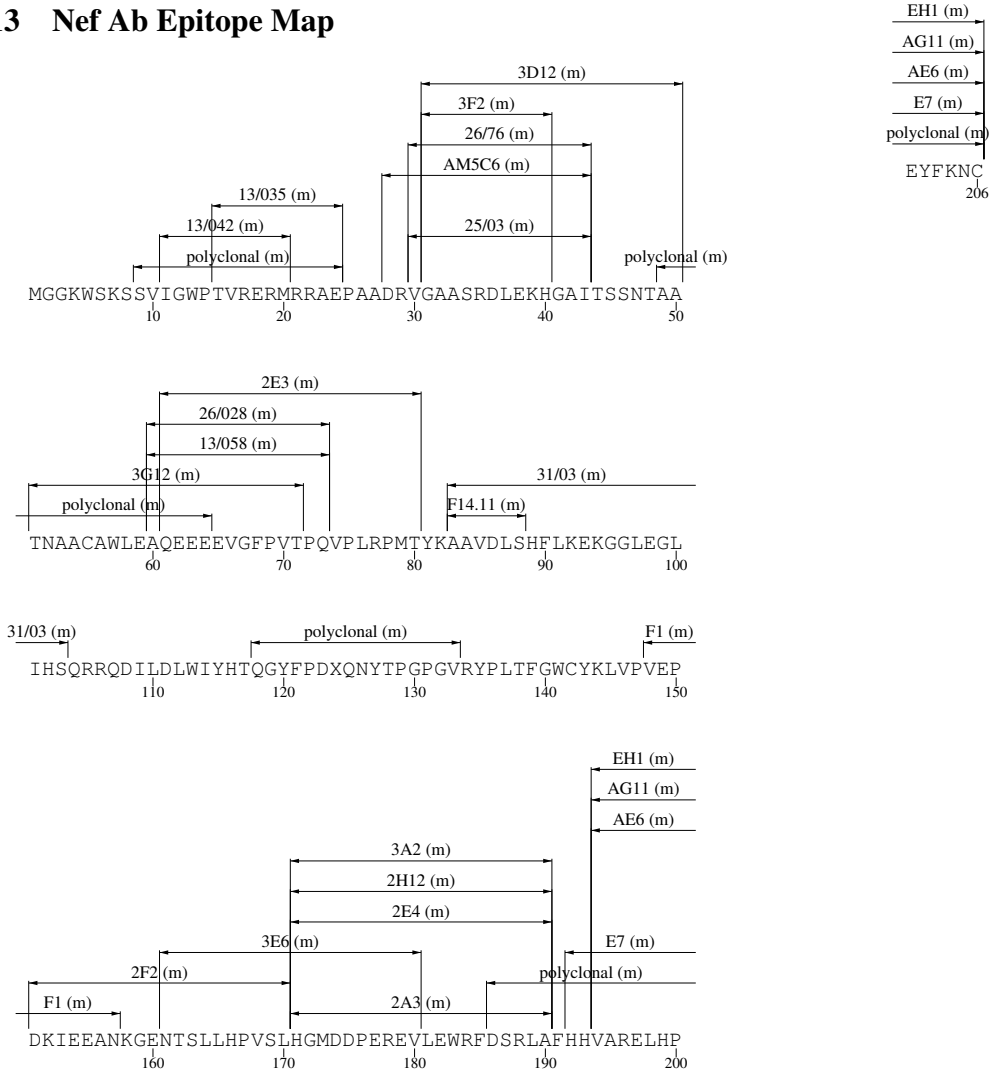
840
850
LERILL
856

IV-D-13 Nef Ab Epitope Map



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Part V

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